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LABORATORY

 **VirginiaTech.**
Biocomplexity Institute

Mathematical and computational foundations of infectious disease epidemiology

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August 7, 2017

Outline

- 1 Goals, History, Basic Concepts
- 2 Dynamics and Analysis
- 3 Surveillance and Forecasting
- 4 Control and optimization
- 5 Putting it all together: theory to practice



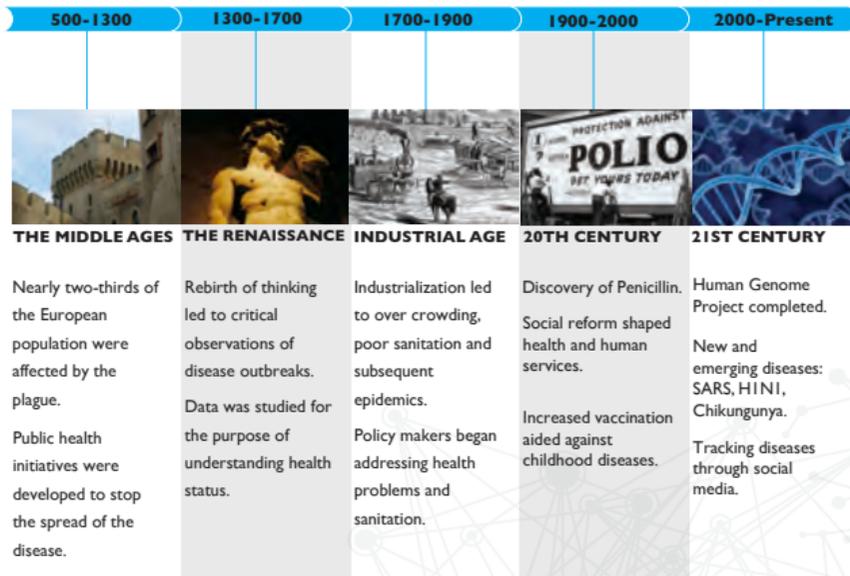
Goals

- **Overview and state of the art** – emphasis on formal models, computing, techniques in algorithms, artificial intelligence, machine Learning and data science
- **Describe open problems and future directions** – aim to attract researchers working in mathematical biology and network science to work in this exciting area
- **Unified framework** based on graphical dynamical systems and associated proof theoretic techniques; e.g. stochastic processes, spectral graph theory, randomized algorithms, mathematical programming, and Bayesian inference.
- **Computational epidemiology** as a multi-disciplinary science
- **Public health epidemiology** as an exemplar of data/computational science for social good
- *Does not aim to be extensive*; references provided for further exploration.
Important topics not covered
 - Validation, verification and uncertainty quantification (UQ)
 - Different kinds of diseases

Epidemics and epidemiology in history

- *Good news:* Pandemic of 1918 lethality is currently unlikely Governments better prepared and coordinated : e.g. SARS epidemic But ..
- Planning & response to even a moderate outbreak is challenging: inadequate vaccines/anti-virals, unknown efficacy, hard logistics issues
- *Modern trends complicate planning:* increased travel, immuno-compromised populations, increased urbanization

HISTORY OF INFECTIOUS DISEASES



- 1918 Pandemic: 50 million deaths in 2 years (3-6% world pop) Every country and community was effected

What is epidemiology?

- Greek words **epi** = *on or upon*; **demos** = *people* & **logos** = *the study of*.¹
- **Epidemiology**: study of the *distribution* and *determinants* of health-related states or events in specified populations, and the *application* of this study to the control of health problems.
Now applies to non-communicable diseases as well as social and behavioral outcomes.
 - *Distribution*: concerned about population level effects
 - *Determinants*: causes and factors influencing health related events
 - *Application*: deals with public health action to reduce the incidence of disease.
- *Computational/mathematical epidemiology*: deals with the development of computational/mathematical methods, tools and techniques to support epidemiology.

¹Last JM, ed. Dictionary of Epidemiology.

Precursors to modern computational epidemiology

BEGINNINGS OF FORMAL EPIDEMIC MODELING

1796



SMALLPOX // Virus

Edward Jenner's research led to the development of vaccines.

Daniel Bernoulli mathematical models demonstrated the benefits of inoculation from a mathematical perspective.

Disease status today: eradicated.

1854



CHOLERA // Bacteria

John Snow was the first to link the London cholera epidemic to a particular water source.

Disease status today: endemic; occurring in poverty-stricken countries.

1897



MALARIA // Parasite

Ronald Ross and George Macdonald developed a mathematical model of mosquito-borne pathogen transmission.

Anderson McKendrick studied with Ross on anti-malarial operations, pioneering many discoveries in stochastic processes.

Disease status today: controlled in US; still prevalent in Africa, India.

1946



TUBERCULOSIS // Bacteria

Albert Schatz discovered the antibiotic streptomycin under the direction of Selman Waksman.

Streptomycin was the first antibiotic that could be used to cure TB.

Disease status today: drug resistant TB strains persist since the 1980s.

1981



HIV // Virus

Luc Montagnier discovered HIV and Robert Gallo determined HIV is the infectious agent responsible for AIDS.

The use of social network models have been initiated with the goal of controlling the virus.

Disease status today: no cure.

Epidemic science in real-time

Editorial, Fineberg and Harvey, Science, May 2009: Epidemics Science in Real-Time

Five areas: (i) Pandemic risk, (ii) vulnerable populations, (iii) available interventions, (iv) implementation possibilities & (v) pitfalls, and public understanding.



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Modeling before an epidemic

(i) Determine the (non)medical interventions required, (ii) feasibility of containment, (iii) optimal size of stockpile, (iv) best use of pharmaceuticals once a pandemic begins

Modeling during an epidemic

(i) Quantifying transmission parameters, (ii) Interpreting real-time epidemiological trends, (iii) measuring antigenic shift and (iv) assessing impact of interventions.

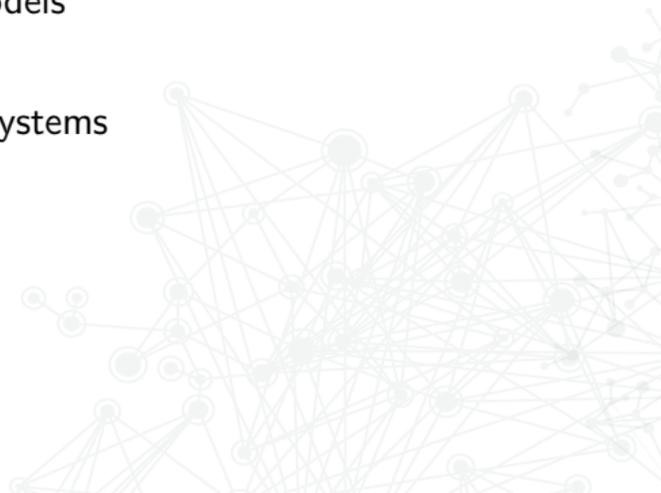


Role of computing, statistics and mathematics in epidemiology

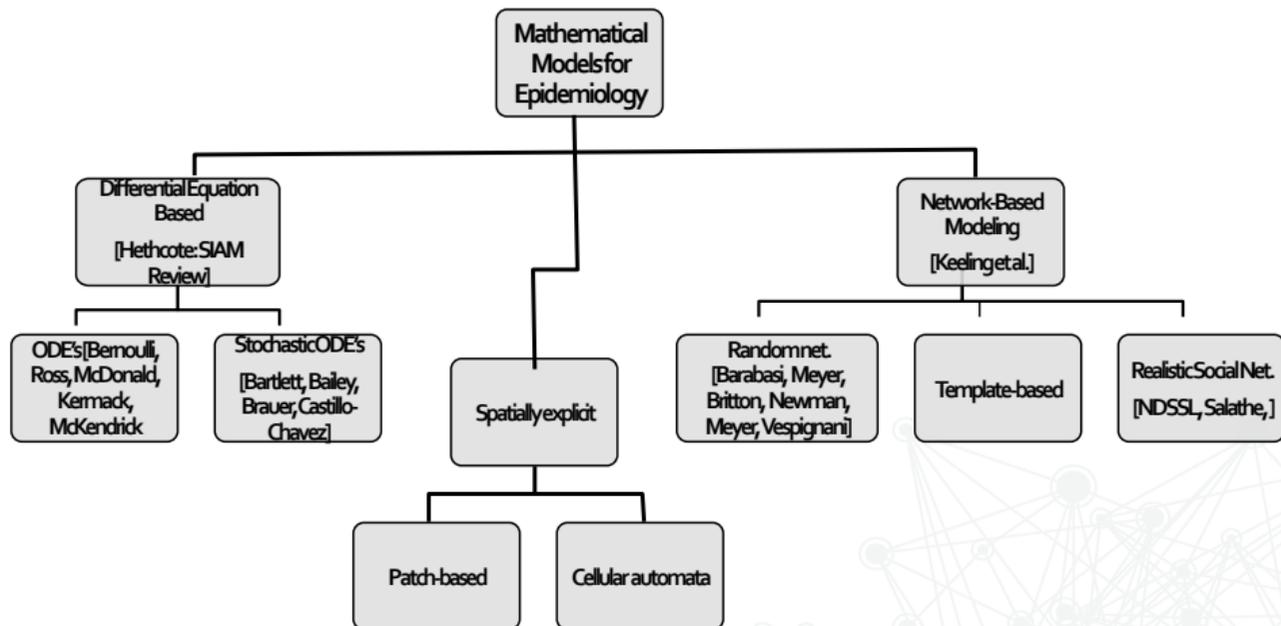
- *Digital Disease Detection: using social media, news and other digital information for improved surveillance, forecasting and nowcasting*
 - Natural language processing, machine learning methods (e.g. matrix factorization)
- *Inference and analysis of Social contact networks and disease parameter*
 - Machine learning (CART trees, PCA)
 - Social and cognitive theories
 - Bayesian inference and graphical models
 - algorithmic graph theory
- *High performance computing & at-scale multi-agent networks*
 - Graphical dynamical systems, e.g. deterministic and probabilistic Boolean networks
 - Markov chain methods
 - Intelligent steering of computational experiments
- *Combinatorial techniques for optimization and control*
 - Algorithmic game theory
 - Markov decision process
 - Mathematical programming
 - Heuristic search

Outline

- Compartmental models
- Networked Epidemiology
 - Branching process
 - Spectral radius characterization
- Extensions: threshold models, voter models
- Competing contagions
- Unifying framework: graph dynamical systems



Classifying formal models

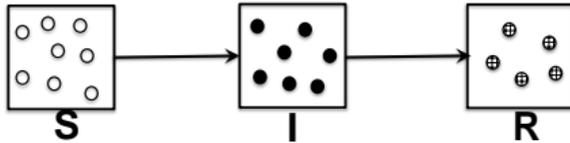


Basic Terminology

- **Susceptibility** – level relative to others of an individual's ability to become infected
- **Exposure** – process that allows infection to pass from infectious to susceptible
- **Infection** – process when pathogen is successfully transmitted to susceptible
- **Recovered** – state following infection

- **Incubation period** – duration between infection and symptoms/infectiousness
- **Infectious period** – duration an individual can transmit disease
- **Transmissibility** – degree to which an infected individual can transmit pathogen to susceptible individuals
- **Symptoms** – physical results of infection, often used in diagnosis of infection

Mass action compartmental Models



Assumption: complete mixing
among population of size N

$$\frac{ds}{dt} = -\beta is$$

$$\frac{di}{dt} = \beta is - \gamma i$$

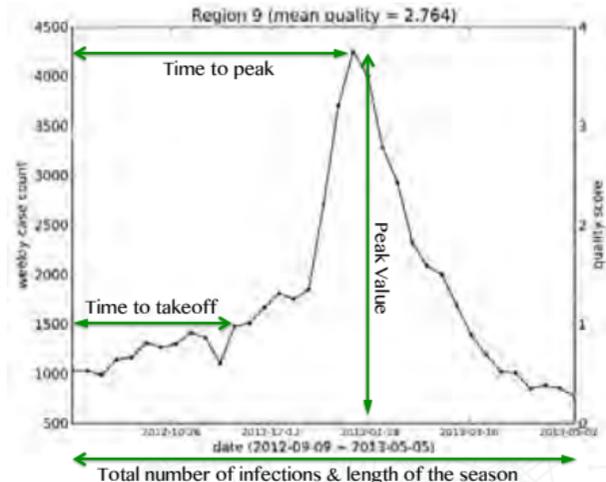
$$\frac{dr}{dt} = \gamma i$$

- *Susceptible* (S): An individual has never had the disease and is susceptible to being infected;
- *Infected* (I): An individual who currently has the disease and can infect other individuals, and
- *Resistant/Recovered* (R): An individual does not have the disease, cannot infect others, and cannot be infected (sometimes called removed)

Basic epidemic quantities

Typical epidemic quantities of interest

- *Epicurve*: time series of the number of infections
- *Peak of the epidemic, time to peak, total number of infections*
- *Basic Reproductive number R_0* : Average number of infections caused by a single infected individual in a completely susceptible population.
 - Condition for epidemic in terms of R_0
- *Take off time*: Time when epidemic takes off
- Time when number of daily infections falls below a threshold



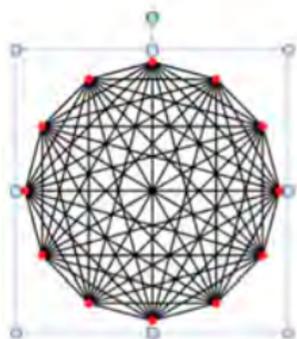
Pros and cons of compartmental models

- Compartmental models have been immensely successful over the last 100 years – (i) workhorse of mathematical epidemiology, (ii) easy to extend and quick to build; (iii) good solvers exist, simple ones can be solved analytically; (iv) mathematical theory of ODEs is well developed
- SARS was estimated to have $R_0 \in [2.2, 3.6]^2$
 - Though it spread across many countries, small number of infections
 - Estimates were based on infections in crowded hospital wards, where complete mixing assumption was reasonable
- Compartmental models lack agency and heterogeneity of contact structure
 - True complexity stems from interactions among many discrete actors
 - Each kind of interaction must be explicitly modeled
 - Refinement is difficult
- Human behavioral issues – Inhomogeneous compliance; changes in the face of crisis
- Harder to design implementable interventions.

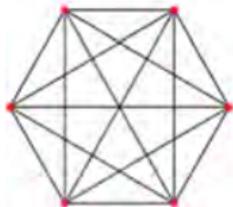
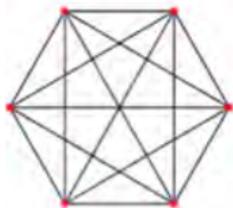
²Lipsitch et al., *Science*, 2003; Riley et al., *Science*, 2003

Illustrating the problem using compartmental models: Impact of interventions

Many ways one can reduce transmission by 50%



Original group of people in contact



Split into 2 equal groups

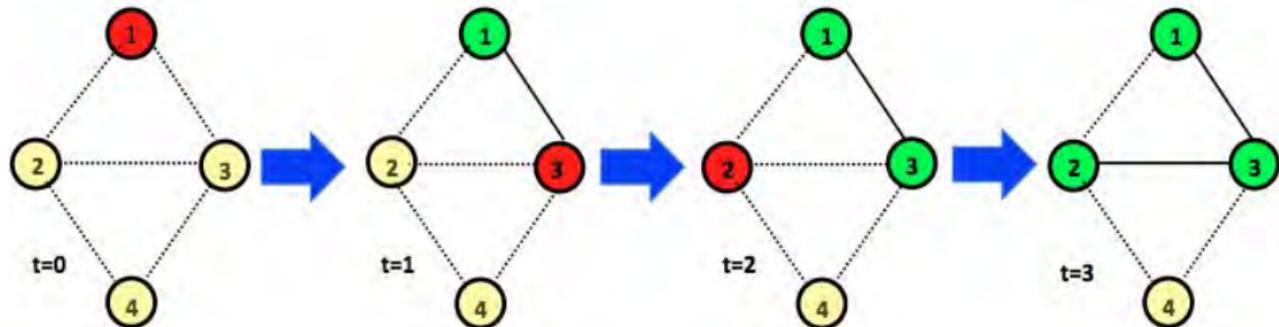


Split into a few unequal groups



Reduce likelihood of transmission

Networked epidemiology: Discrete time SIR model on a network

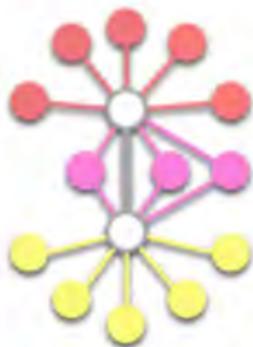


Fixed point: $R = \{1, 2, 3\}$ and $S = \{4\}$

$$p(1, 3)(1 - p(1, 2))p(2, 3)(1 - p(2, 4))(1 - p(3, 4))$$

- Each node is in states S (susceptible), I (infectious) or R (recovered)
- Time is discrete
- Each infected node u spreads the infection independently to each susceptible neighbor v with probability $p(u, v)$
- Infected node u recovers after 1 time step
- *Fixed point*: all nodes in states S or R

Networks capture heterogeneity

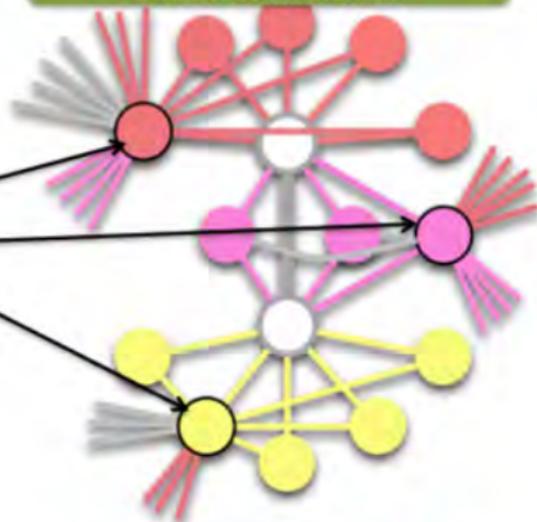


Home School
Other Work

Network for one
small family

Challenging to visualize
dense networks

Additional
contacts for
these
individuals



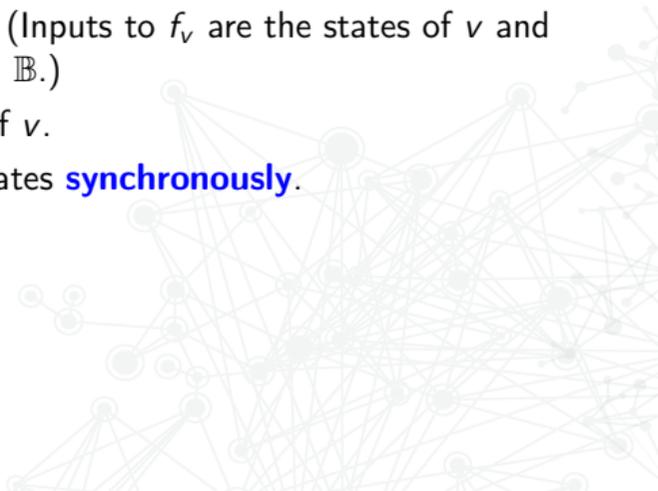
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A general computational framework:
graphical models of dynamical (multi-agent) systems



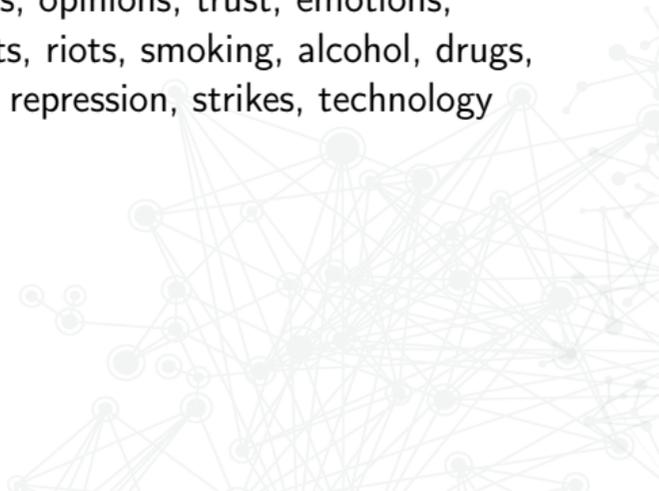
Graphical Dynamical Systems (GDS)

- Useful abstract model for networked interaction systems.
- Components of a GDS \mathcal{S} :
 - Undirected graph $G(V, E)$.
 - A state value from a finite domain \mathbb{B} for each vertex v . (We use $\mathbb{B} = \{0, 1\}$.)
 - A local function f_v for each vertex v . (Inputs to f_v are the states of v and its neighbors; the output of f_v is from \mathbb{B} .)
 - The value of f_v gives the next state of v .
 - Vertices compute and update their states **synchronously**.



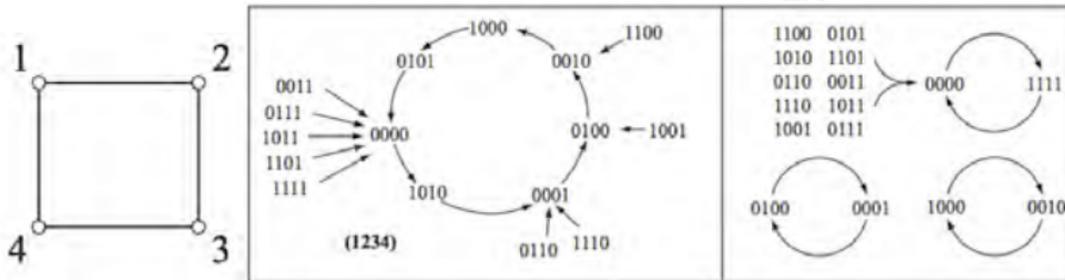
Contagions as graphical dynamical systems

- Contagion: (Cont = together with & Tangere = to touch): General term used to denote spread of “something” via interaction between agents
- Examples: financial contagion, product contagion, social contagion, malware contagion.
- Examples in social domain: rumors, fads, opinions, trust, emotions, ideologies, information, mass movements, riots, smoking, alcohol, drugs, contraceptive adoption, financial crises, repression, strikes, technology adoption



Example: Phase space of \mathcal{S}

- Directed graph with one vertex for each possible configuration.
- Directed edge (x, y) if the system transitions from the configuration corresponding to x to the one corresponding to y in one time step.
- Captures the **global behavior** of the system.
- Size of the phase space is **exponential** in the size of the SyDS.
- When the local functions are probabilistic, the phase space is best represented as a *Markov chain* (which is exponentially larger than the description).



Each node computes a Boolean NOR

Computational problems for GDS \mathcal{S} , phase space $\mathcal{P}(\mathcal{S})$, noisy observation \mathcal{O}

Analysis Problems

Does $\mathcal{P}(\mathcal{S})$ have a fixed point, GE configuration, transient of length $\geq k$?

Inference Problem

Find the most likely: (i) initial configuration, (ii) the transmission tree, (iii) underlying network or (iv) disease parameters

Optimization Problems

Remove/Modify $\leq K$ nodes/edges in G so as to infect minimum number of nodes.

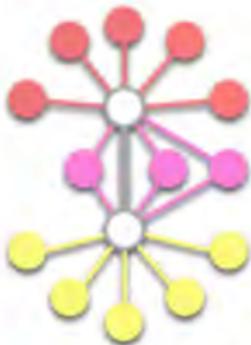
Forecasting and Situational Assessment

Assess total number of nodes in a particular state, Forecast total number of nodes (probabilistically) in a particular state after time t

Mapping epidemic problems onto GDS problems

Quantity/Problem in epidemiology	GDS analogue
Epicurve	Analysis (e.g., #1's in configuration) of phase space trajectory
Computing epidemic characteristics	Analysis problem: Reachability problem in GDS
Inferring index case, given information about graph and observed infections	Predecessor inference problems in GDS
Inferring disease model, given the graph and observed infections	Local function inference problem

Networks capture heterogeneity

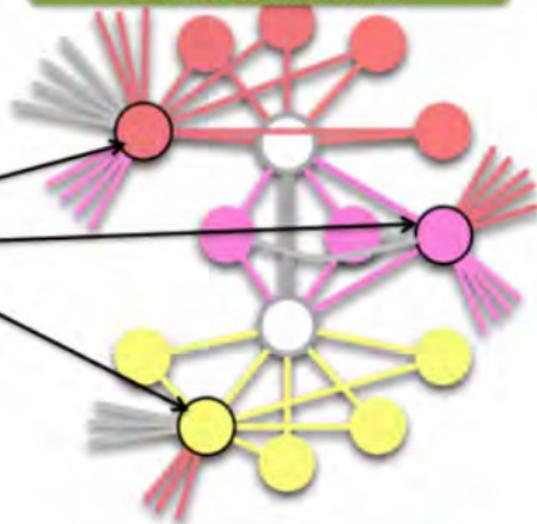


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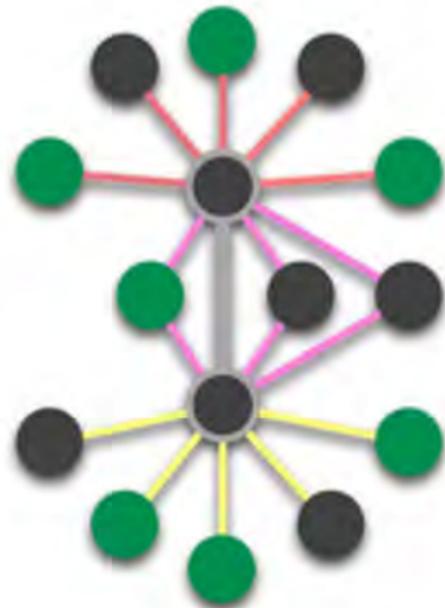
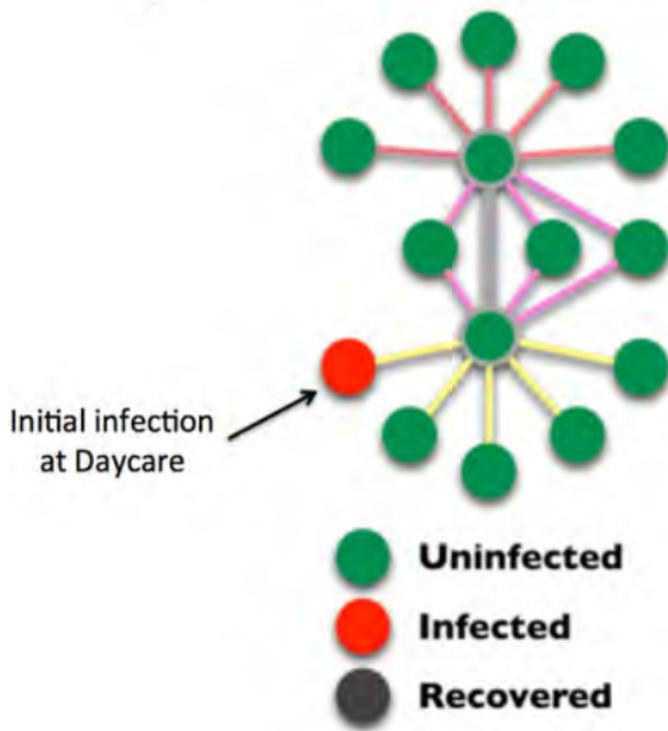
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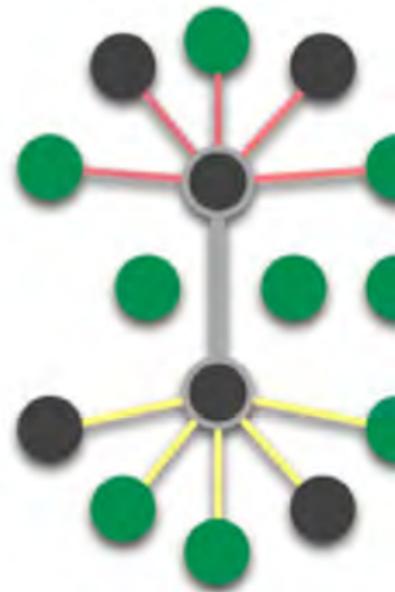
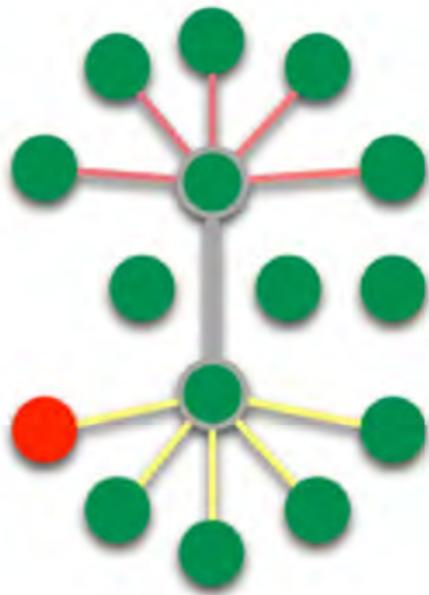
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Unmitigated disease spread



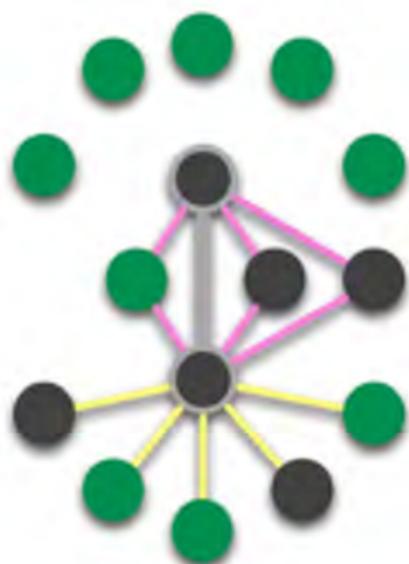
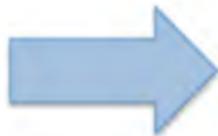
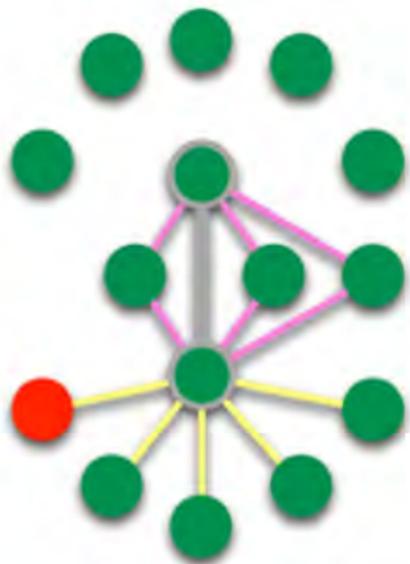
Intervention: Social Distancing

Compliant individuals don't engage in other activities (non-home, work, school)



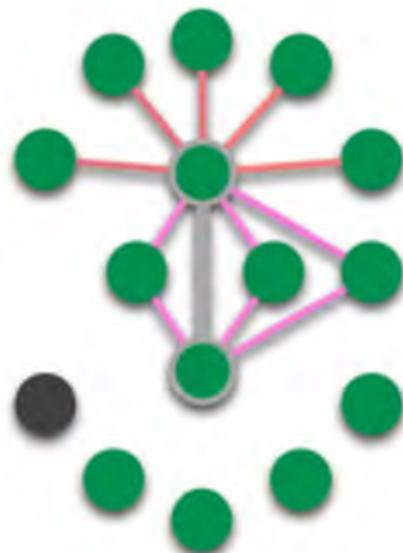
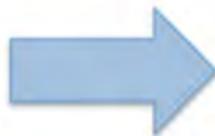
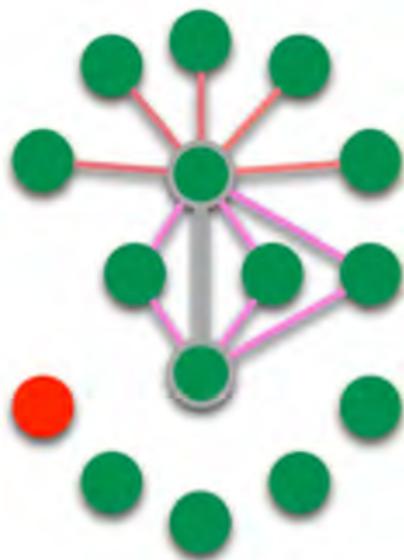
Intervention: Close Work

Compliant individuals don't go to work



Intervention: Close Schools

Compliant individuals don't go to school



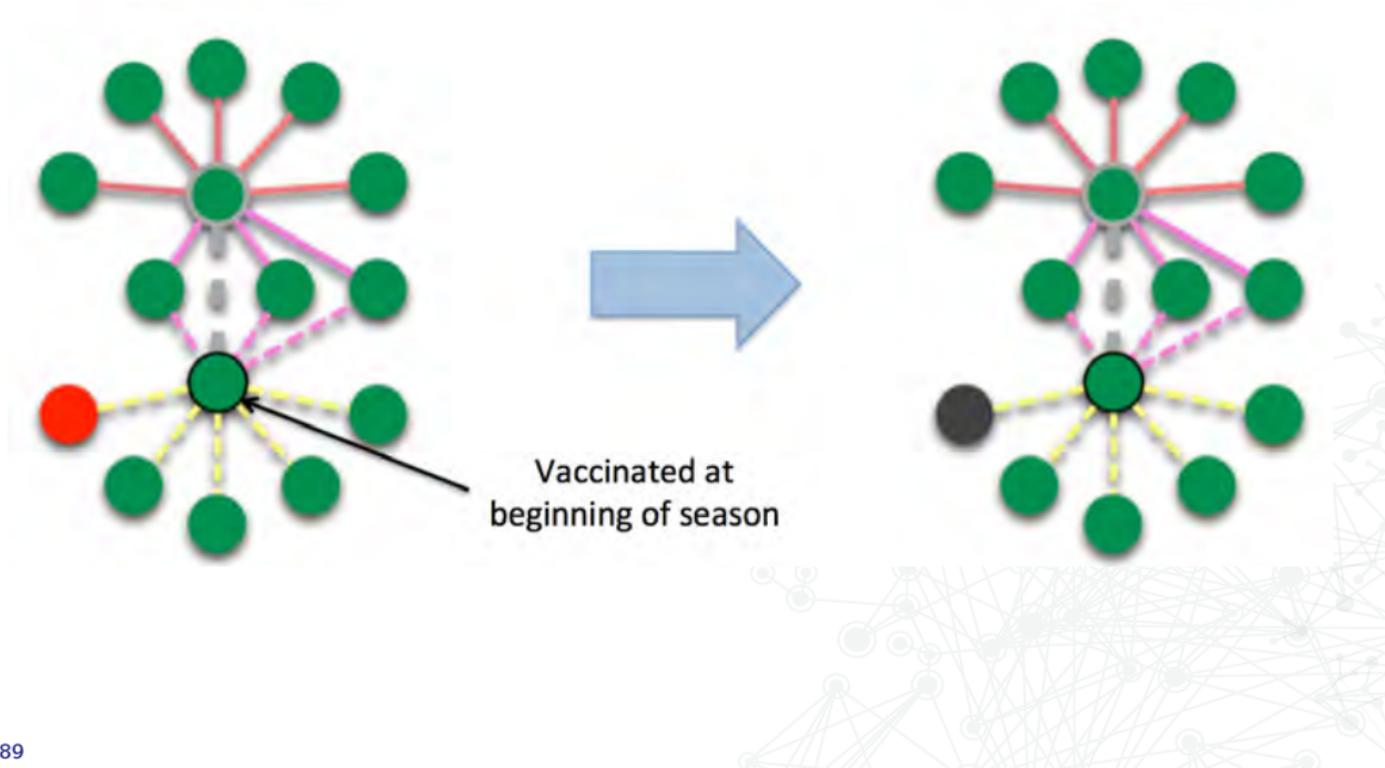
Intervention: Pharmaceuticals

- **Efficacy** – Reduction in transmission from pharmaceutical
- **Regimen duration** – Duration a pharmaceutical is active in an individual
- **Supply** – Pharmaceuticals are finite and logistical constraints can limit availability



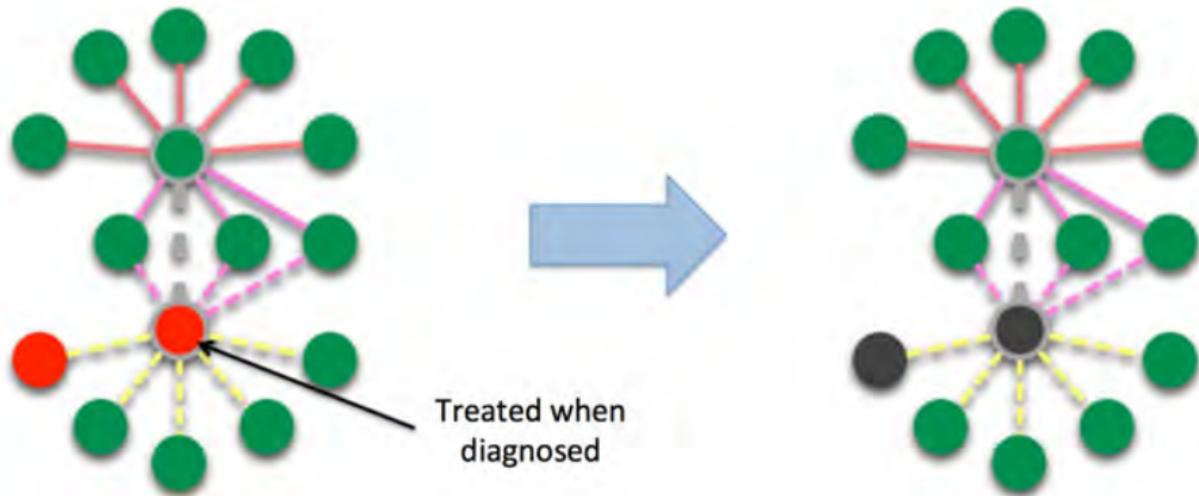
Intervention: Vaccination

Vaccine administered: Delay till full efficacy, provides effect throughout simulation following administration



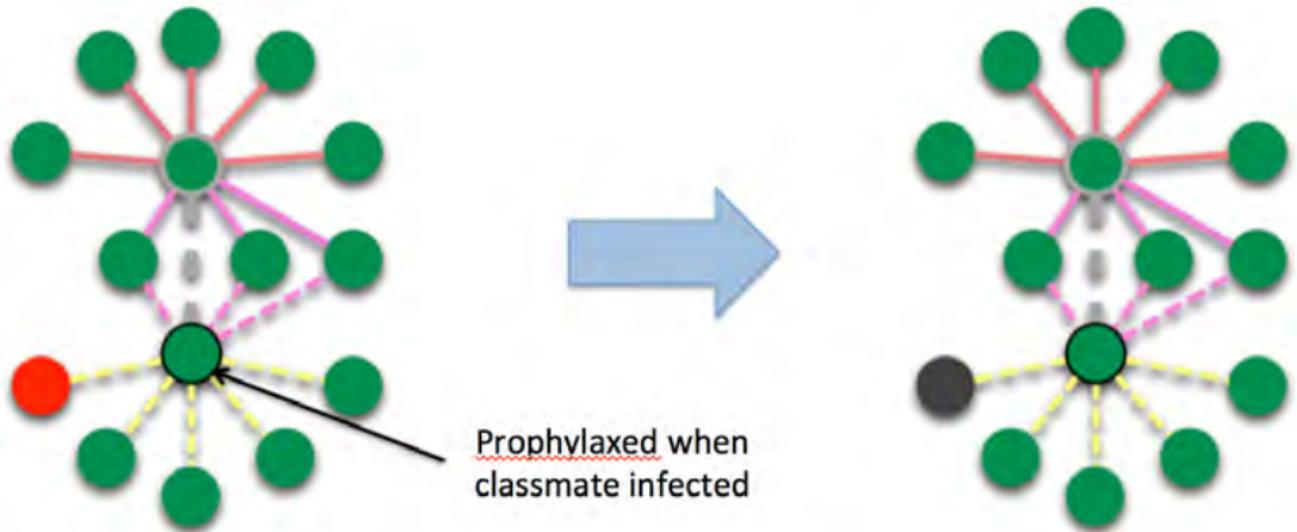
Intervention: Treatment

Administering medicine upon diagnosis Shortens symptomatic periods, limits transmissibility



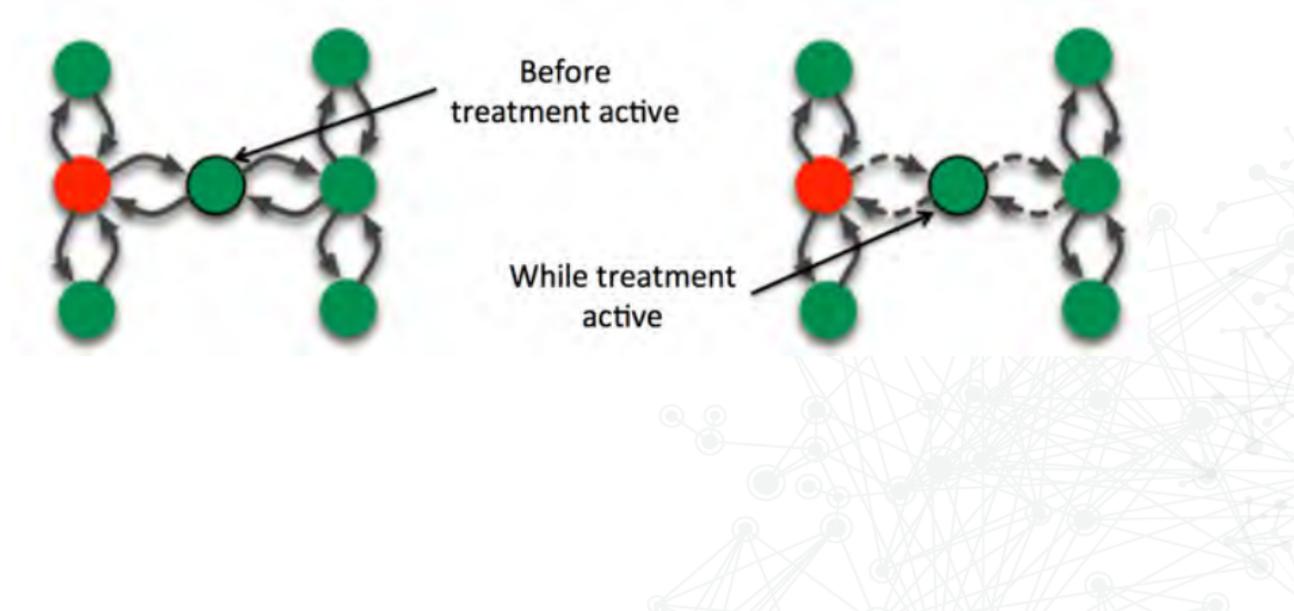
Intervention: Prophylaxis

Providing medicine to those at risk of infection regardless of diagnosis – Only effective will medicine is taken



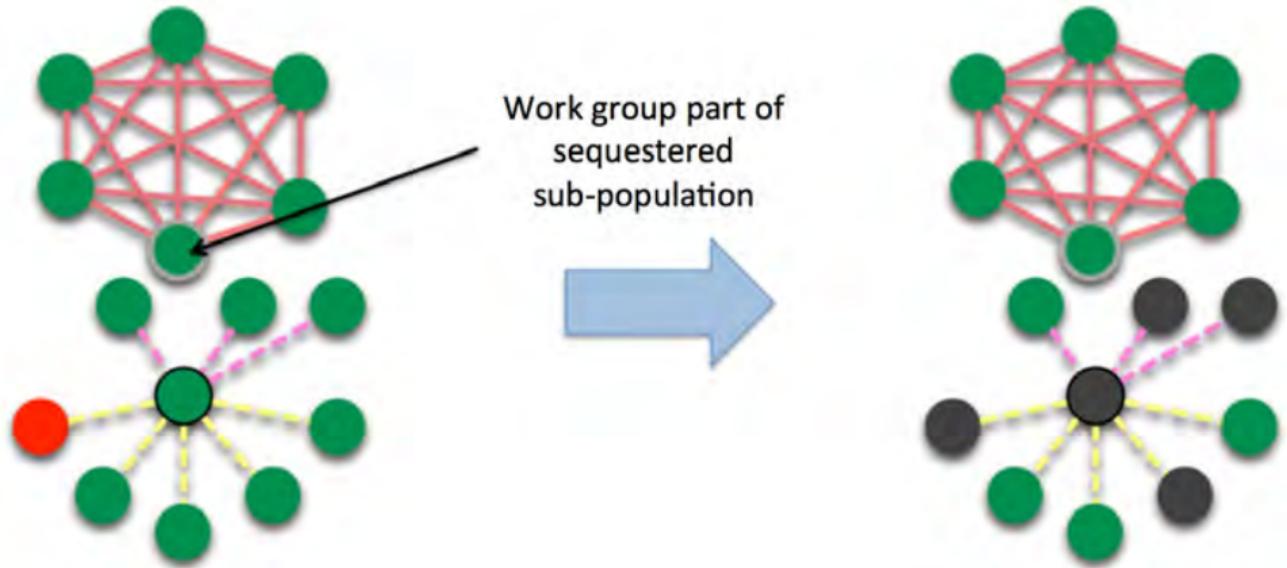
Intervention: Treatment

Each interaction has two probabilities: Likelihood of infection (susceptibility)
& Likelihood of transmission (transmissibility)
Different pharmaceuticals have different effects on these parameters



Intervention: Sequestration

Members of sub-population remove all links except with each other



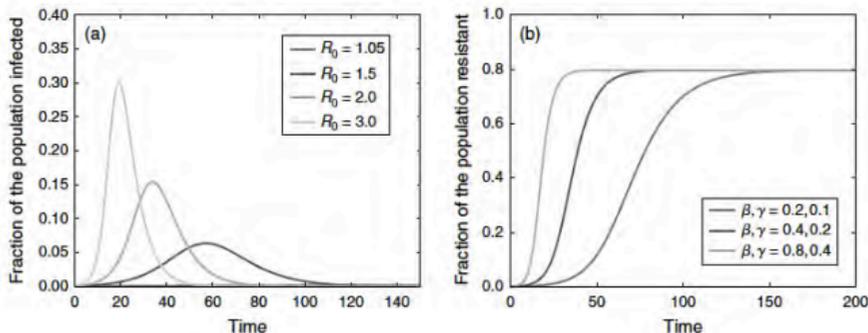
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Dynamics in Compartmental Models

$$\begin{aligned}\frac{ds}{dt} &= -\beta is \\ \frac{di}{dt} &= \beta is - \gamma i \\ \frac{dr}{dt} &= \gamma i\end{aligned}$$

- $\frac{di}{dt} > 0$ (leads to a large epidemic) if $\frac{\beta s}{\gamma} > 1$
- At the start of epidemic: $s \approx 1$
- $R_0 = \beta/\gamma$: reproductive number
- Large epidemic if and only if $R_0 > 1$
- Modeling epidemic = estimating R_0
- Controlling epidemic: reducing R_0



Effect of R_0 on the dynamics³

³Dimitrov and Meyers, *INFORMS*, 2010

Dynamics over GDS: Trees



- Assume graph is an infinite d -ary tree, with transmission probability p on each edge. Using branching process as a proof technique.
- Assume the root is the only infected node, and everything else is susceptible
- Let q_n be the probability that the disease survives for at least n waves (level of tree), in other words, that at least one individual in the n^{th} level of the tree becomes infected.
- $q^* = \lim_{n \rightarrow \infty} q_n$

Theorem

Let $R_0 = pd$. If $R_0 < 1$ then $q^* = 0$. If $R_0 > 1$, then $q^* > 0$.

Image from: D. Easley and J. Kleinberg, 2010.

Dynamics and analysis on general graphs



Dynamics in the SIR model on other networks: impact of structure

- Phase transition for SIR model shown in many graph models: there exists a threshold p_t such that few infections if $p < p_t$ but large outbreak if $p > p_t$
- Technique: mainly extends branching process
- Clique on n nodes⁴: $p_t = 1/(n - 1)$
- Lattice \mathbb{Z}^d : $p_t \rightarrow 1/(2d)$, as $d \rightarrow \infty$
- Random d -regular graphs: $p_t = 1/d$
- Not well understood in general graphs
 - Partial characterization in finite regular expander graphs with high girth⁵
 - Characterization in terms of the second moment⁶

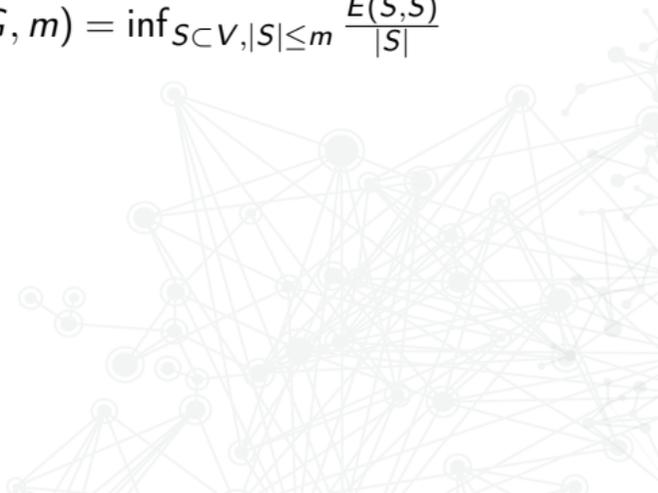
⁴Erdős and Rényi, 1959

⁵Alon, Benjamini and Stacey, 2001

⁶Chung, Horn, Lu, 2009

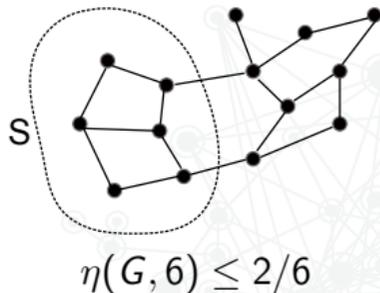
Dynamics in the SIS model: preliminaries

- Nodes in Susceptible (S) or Infectious (I) states
- Each infected node spreads infection to each susceptible neighbor with rate β
- Each infected node becomes susceptible with rate δ
- $\rho(A)$: spectral radius of adjacency matrix A
- $T = \delta/\beta$
- Generalized isoperimetric constant: $\eta(G, m) = \inf_{S \subset V, |S| \leq m} \frac{E(S, \bar{S})}{|S|}$



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- Generalized isoperimetric constant: $\eta(G, m) = \inf_{S \subset V, |S| \leq m} \frac{E(S, \bar{S})}{|S|}$
- Spectral radius
 $\rho(A) = \max_x x^T A x / x^x$
- Avg degree $\leq \rho(A) \leq \Delta(G)$,
where $\Delta(G)$ is the maximum node degree



Dynamics in the SIS model (informal) spectral characterization⁹

- $\rho(A)$: spectral radius of adjacency matrix A
 - $T = \delta/\beta$
 - Generalized isoperimetric constant: $\eta(G, m) = \inf_{S \subset V, |S| \leq m} \frac{E(S, \bar{S})}{|S|}$
- If $\rho(A) < T$: epidemic dies out “fast”
- If $\eta(m) > T$: epidemic lasts “long”

Similar implications but different assumptions, extended to SEIR models^{7 8}

⁷BA Prakash, D Chakrabarti, M Faloutsos, N Valler, C Faloutsos. *Knowledge and Information Systems*, 2012

⁸Y. Wang, D. Chakrabarti, C. Wang and C. Faloutsos, *ACM Transactions on Information and System Security*, 2008.

⁹A. Ganesh, L. Massoulié and D. Towsley, *IEEE INFOCOM*, 2005

Lemma (Sufficient condition for fast recovery)

Suppose $\rho(A) < T$. Then, the time to extinction τ satisfies

$$E[\tau] \leq \frac{\log n + 1}{1 - \rho(A)/T}$$

Lemma (Sufficient condition for lasting infection)

If $r = \frac{\delta}{\beta\eta(m)} < 1$, then the epidemic lasts for “long”:

$$\Pr[\tau > r^{-m+1}/(2m)] \geq \frac{1-r}{e}(1 + O(r^m))$$

Implications for different network models

- Hypercube: $\rho(G) = \log_2 n$, and $\eta(m) = (1 - a) \log_2 n$ for $m = n^a$
 - Fast die out if $\beta < \frac{1}{\log_2 n}$, slow die out if $\beta > \frac{1}{(1-a) \log_2 n}$
- Erdős-Rényi model: $\rho(G) = (1 + o(1))np = (1 + o(1))d$ and $\eta(m) = (1 + o(1))(1 - \alpha)d$ where $m/n \rightarrow \alpha$
 - Fast die out if $\beta < \frac{1}{(1+o(1))d}$, slow die out if $\beta > \frac{1}{(1+o(1))(1-\alpha)d}$
- Power law graphs (Chung-Lu model): assume degree distribution with power law exponent $\gamma > 2.5$
 - $E[\tau] = O(\log n)$ if $\beta < (1 - u)/\sqrt{m}$ and $E[\tau]$ exponential if $\beta > m^\alpha/\sqrt{m}$ for some $u, \alpha \in (0, 1)$ and $m = n^\lambda$, for $\lambda \in (0, \frac{1}{\gamma-1})$

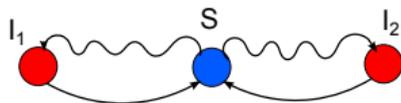
Implications for different network models

- In general, gap between necessary and sufficient conditions for epidemic to last long
- Similar implications through different assumptions, extended to SEIR models^{10 11}

¹⁰Y. Wang, D. Chakrabarti, C. Wang and C. Faloutsos, *ACM Transactions on Information and System Security*, 2008.

¹¹BA Prakash, D Chakrabarti, M Faloutsos, N Valler, C Faloutsos. *Knowledge and Information Systems*, 2012

Competing contagions in the SIS model: the $S I_1 I_2 S$ model



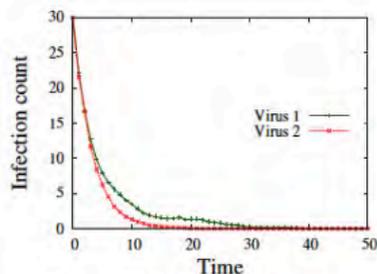
- $G = (V, E)$: undirected contact graph
- State transition for node u from S to I_j at rate β_j , $j = 1, 2$, depending on which infected neighbor of u is successful in infecting it
- Nodes switch back to susceptible state at rate δ_j from I_j to S
- What is the limiting distribution?

Steady state distribution in SI_1I_2S model: “winner takes all”

Theorem

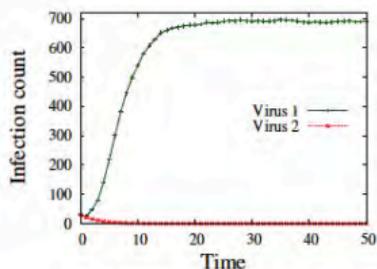
^a In the SI_1I_2S model in graph G with adjacency matrix A , and parameters $(\beta_1, \beta_2, \delta_1, \delta_2)$, virus 1 will dominate and virus 2 will completely die-out in the steady state if $\lambda_1 \frac{\beta_1}{\delta_1} > 1$ and $\frac{\beta_1}{\delta_1} > \frac{\beta_2}{\delta_2}$

^aB. Aditya Prakash, A. Beutel, R. Rosenfeld, C. Faloutsos, WWW, 2012



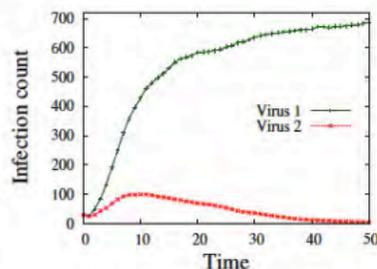
(a) BELOW (Time-plot)

Both viruses below threshold: $\lambda_1 \frac{\beta_1}{\delta_1} < 1$, $\lambda_1 \frac{\beta_2}{\delta_2} < 1$



(b) MIXED (Time-plot)

Virus 1 above threshold, virus 2 below: $\lambda_1 \frac{\beta_1}{\delta_1} > 1$, $\lambda_1 \frac{\beta_2}{\delta_2} < 1$



(c) ABOVE (Time-plot)

Both above threshold: $\lambda_1 \frac{\beta_1}{\delta_1} > 1$, $\lambda_1 \frac{\beta_2}{\delta_2} > 1$, $\frac{\beta_1}{\delta_1} > \frac{\beta_2}{\delta_2}$

- 1 Goals, History, Basic Concepts
- 2 Dynamics and Analysis
- 3 Surveillance and Forecasting**
- 4 Control and optimization
- 5 Putting it all together: theory to practice



Surveillance and Forecasting

What we will cover in this section

- Forecasting flu case counts using data-driven methods
- Forecasting flu epicurve characteristics
- Spatio-temporal models with applications to disease surveillance.

Breaking down the AI topics of interest

- Robust Information extraction
 - short text, long text, images
- Robust dynamic regressions
- Data Assimilation methods



Syndromic surveillance

Traditional vs syndromic surveillance

- Traditional: laboratory tests of respiratory specimens, mortality reports
- Syndromic: 'clinical features that are discernable before diagnosis is confirmed or activities prompted by the onset of symptoms as an alert of changes in disease activity' ¹²

Issues in considering a syndromic surveillance system

- Sampling bias
- Veracity and reliability of syndromic data
- Granularity of space- and time-resolution
- Change point detection versus forecasting

Broad consensus is that syndromic surveillance provides some early detection and forecasting capabilities but nobody advocates them as a replacement for traditional disease surveillance.

¹²K Hope, DN Durrheim, ET d'Espaignet, C Dalton, *Journal of Epidemiology and Community Health*, 2006

Surrogate data sources: the good, bad, and ugly

Proposals for flu surveillance

- Search queries

'Miley Cyrus cancels Charlotte Concert over Flu'



- OTC medication sales

Discount sales, hoarding, lack of patient-specific data



- Wikipedia page views

Lack of specificity about visitor locations



- Twitter

Concerned awareness tweets versus infection reporting tweets



Surrogate data sources: the good, bad, and ugly

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- Twitter

Concerned awareness tweets versus infection reporting tweets



Self-reinforcing and self-defeating prophecies abound!

Google Flu Trends

Google Flu Trends (<http://www.google.org/flutrends/>) is a nowcasting system for monitoring health-seeking behavior through Google queries. ¹³

- 50 million candidate queries were narrowed down to a set of 45 (proprietary) queries that most accurately fit CDC ILI data in the US
- Queries merely correlated with flu season (e.g., 'high school basketball') were hand pruned
- Relative query volumes (w.r.t. weekly search volume per location) were used as independent variables
- Simple linear model from query fraction \mapsto ILI physician visits.

$$\text{logit}(P) = \beta_0 + \beta_1 \times \text{logit}(Q) + \varepsilon \quad (1)$$

where P is the percentage of ILI related physician visits and Q is the ILI-related search query fraction.

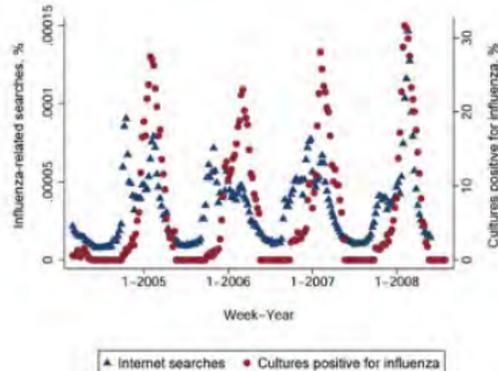


¹³J Ginsberg, MH Mohebbi, RS Patel, L Brammer, MS Smolinski, L Brilliant, *Nature*, 2008

Was Google Flu Trends a pioneer?

Polgreen et al.¹⁴ was the original paper that proposed the use of search queries for influenza surveillance

- Yahoo search queries from March 2004–May 2008
 - 1 Fraction of US search queries that contain the term 'influenza' or 'flu' but NOT 'bird', 'avian', or 'pandemic'
 - 2 Fraction of US search queries that contain 'influenza' or 'flu' but NOT 'bird', 'avian', 'pandemic', 'vaccination', or 'shot'
- Explored searches with one- to ten-week lead times as explanatory variables; reports 1-3 week lead time over CDC reporting

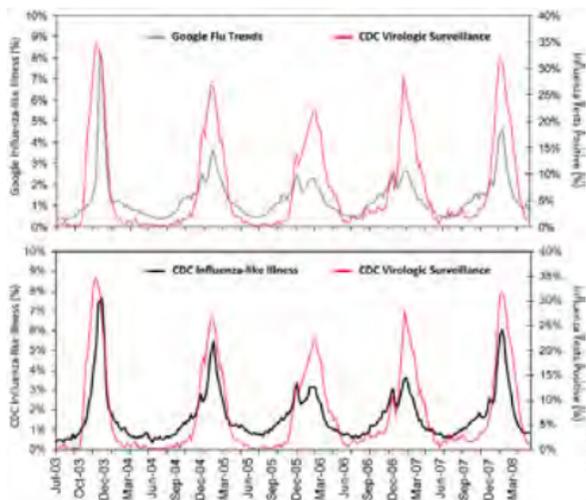


¹⁴PM Polgreen, Y Chen, DM Pennock, FD Nelson, *Clinical Infectious Diseases*, 2008

Google Flu Trends vs. traditional surveillance

Comparisons of GFT as well as CDC ILI surveillance data against US Influenza Virologic Surveillance data ¹⁵

- First study evaluating Google Flu Trends against laboratory confirmed infections
- Pearson correlation coefficients:
GFT-Virological (0.72),
CDC/ILI-Virological (0.85), GFT-CDC/ILI (0.94)

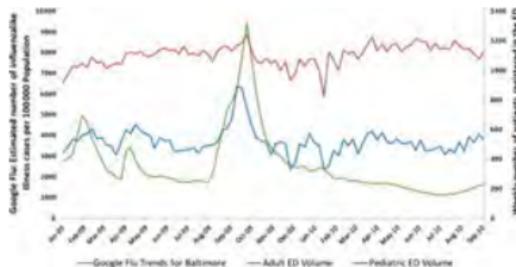


¹⁵JR Ortiz, H Zhou, DK Shay, KM Neuzil, AL Fowkes, CH Goss, *PLoS ONE*, 2011

Google Flu Trends w/ other data sources

How does GFT fare when used in conjunction with other indicators? ¹⁶

- 5 typical seasons (2004–2008, 2010–2011) and 2 atypical seasons (2008–2009 and 2009–2010) studied in an urban tertiary care provider in Baltimore, MD
- Response variable: influenza-related ED visits; independent variables: GFT, local temperature, local relative humidity, Julian weeks; connected using a GARMA model



- Autoregressive component had the strongest influence

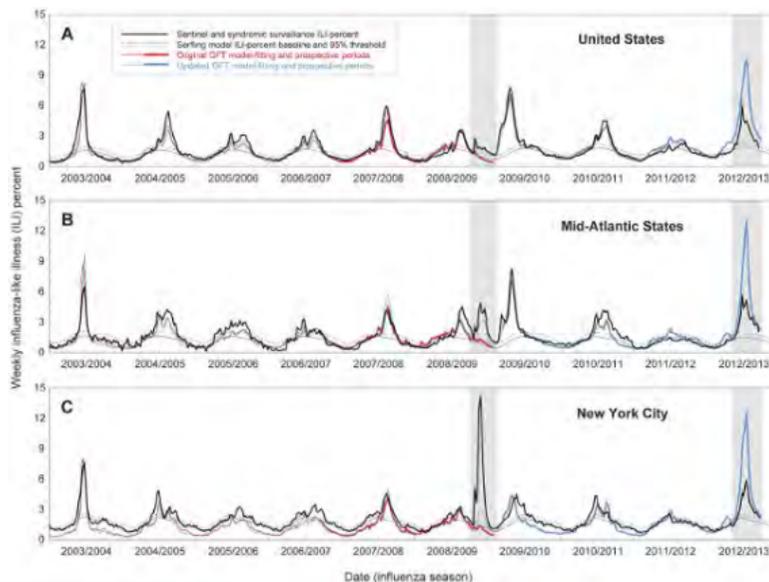
¹⁶AF Dugas, YH Hseih, SR Levin, JM Pines, DP Mareiniss, A Mohareb, CA Gaydos, TM Perl, RE Rothman, *Clinical Infectious Diseases*, 2012

More murmurs of discontent

GFT evaluated at three geographic scales: national (US), regional (mid-Atlantic), and local (NY city) levels ¹⁷

■ Correlations can be misleading

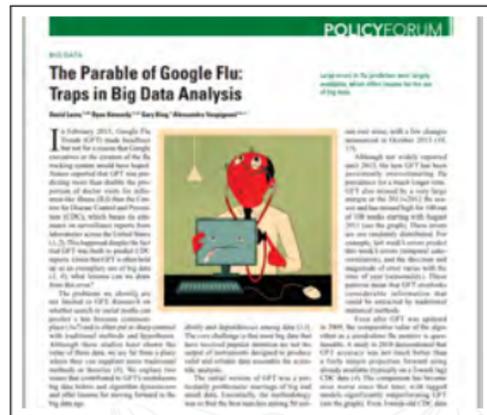
- 1 GFT completely missed the first wave of the 2009 H1N1 pandemic flu
- 2 GFT overestimated the intensity of the H3N2 epidemic during 2012–2013



¹⁷DR Olson, KJ Konty, M Paladini, C Viboud, L Simonsen, *PloS computational biology*, 2013

- Search algorithm continually being modified
- Additional search term suggestions
- Lack of transparency
- Big data 'hubris'

For the two years ending Sep 2013, Google's estimates were high in 100 out of 108 weeks. After Oct 2013 update, Google's estimates are over by 30% for 2013–2014 season



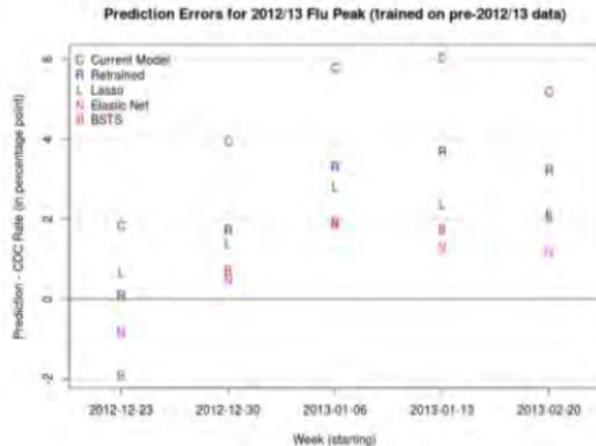
¹⁸DM Lazer, R Kennedy, G King, A Vespignani, *Science*, 2014

¹⁹DM Lazer, R Kennedy, G King, A Vespignani,

http://gking.harvard.edu/files/gking/files/ssrn-id2408560_2.pdf, 2014

Recent improvements to Google Flu Trends²⁰

- Handling 'inorganic queries' resulting from heightened media coverage - spike detectors (long term and short term).
- Handling drift
 - Retraining after each season
 - Use of regularizers



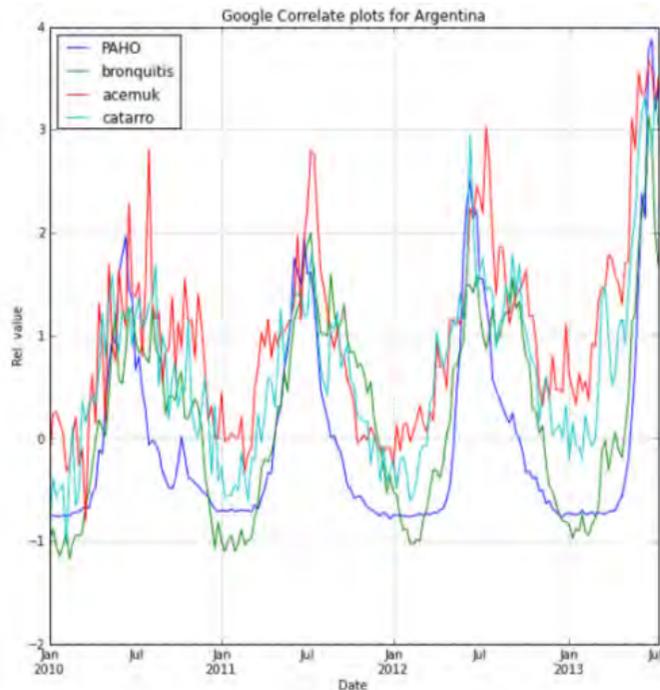
²⁰<http://patrickcopeland.org/papers/isntd.pdf>

Designing your own vocabulary²¹

- Pseudo-query expansion methods
 - Health ministry website.
 - News articles.
- Google Correlate
 - Correlate search query volumes with disease case count time series.
 - Compare against different time shifted case counts.
- Example keywords
 - From search query words such as 'flu',
 - through correlation analysis words we can discover such as 'ginger.'

²¹P Chakraborty, P Khadivi, B Lewis, A Mahendiran, J Chen, P Butler, EO Nsoesie, SR Mekaru, JS Brownstein, M Marathe, N Ramakrishnan, *SDM*, 2014

Designing your own vocabulary (contd..)



Symptomatic words:

“bronquitis”, “catarro”, “tos seca”
(whooping cough)

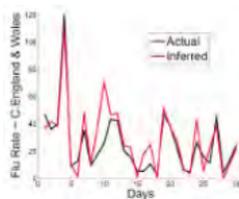
Medicinal words: “acemuk”,
“claritromicina” (clarithromycin)

Interesting words: ginger
 (“jengibre”), leave letter (“letra de
deja”)

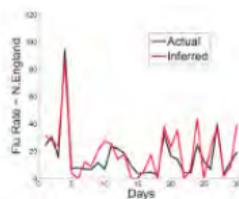
Nowcasting with Twitter

Culotta²² and Lamos et al.²³ adapted GFT-like ideas to forecasting ILI case counts using Twitter

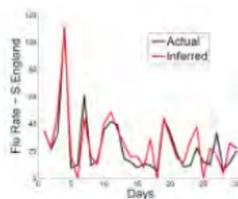
- Geolocation to narrow down to regions of interest
- Document filtering to first identify ILI-related tweets
- Prediction models:
 - 1 Regression with multiple keyword independent variables performs better than simple linear regression (as used in GFT)
 - 2 LASSO with n-grams as features



(a) C. England & Wales - RMSE: 11.781



(b) N. England - RMSE: 9.757



(c) S. England - RMSE: 9.599

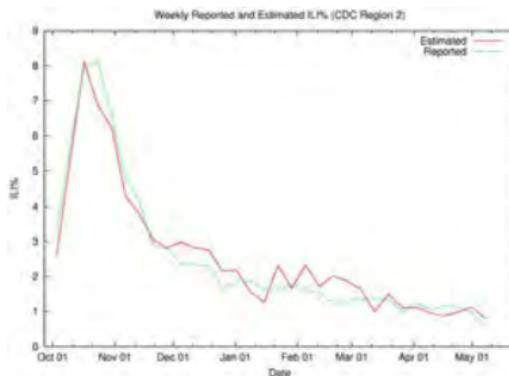
²²A Culotta, *Proceedings of the First Workshop on Social Media Analytics*, 2010

²³V Lamos, N Cristianini, *ACM TIST*, 2012

Using Twitter during the H1N1 pandemic

Signorini et al. ²⁴ study the use of Twitter to nowcast the 2009 season.

- Geolocated tweets (US home locations) containing specific flu-related keywords were filtered and used to create a dictionary (after stemming, stopword removal]
- Support vector regression from dictionary to CDC ILI rates
- Model trained on 9 of the 10 CDC US regions and evaluated on the 10th



²⁴A Signorini, AM Segre, PH Polgreen, *PLoS One*, 2011

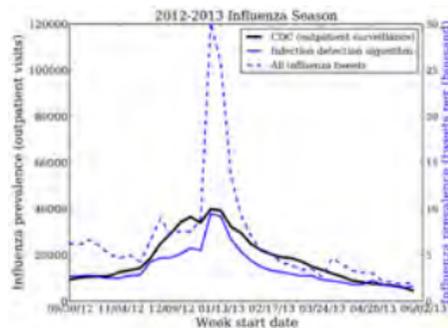
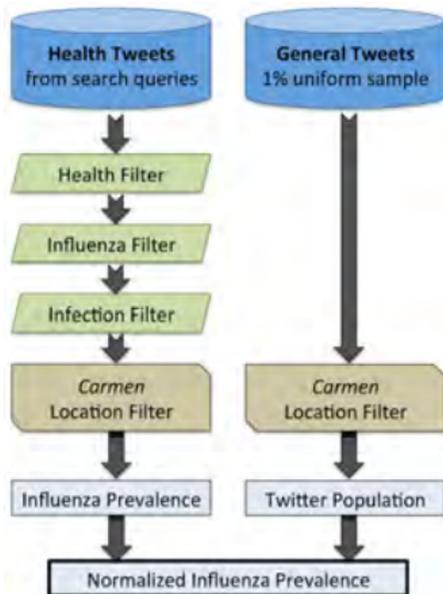
- Coding rules to help categorize tweets
- 52.6% of tweets were about news and information; 4.5% were misinformation

Table 1. Descriptions and Examples of Content Categories.

Content	Description	Example Tweets
Resource	Tweet contains a URL, video, audio, or information. May be the title or summary of the linked article. Content may or may not be factual.	"Chris Brown: First Case of Sars-CoV-2 (New York Times) is an eye-roller near what the West is doing in Chicago. It's important to understand." "Wasn't it about the fact that the virus is spreading globally?"
Personal Experience	Tweeter user mentions a direct personal or indirect (e.g., friend, family, acquaintance) experience with the COVID virus or the consequences, effects of COVID.	"Since its peak almost appeared my front yard as I'd see the bird from the air and on top of it was I." "It's not just a virus to health, it's the height of the bird." "It's not just a virus to."
Personal Opinions and Views	Tweeter user gives their opinion of the COVID virus/situation, news, or response it used for an experience of information. Content is not related to commentary.	"There's people who said from March to the start of the year a health crisis in 2020 would be the end of the world." "Currently looking up some info on COVID." "Sars-CoV-2 virus."
Users' Health	Tweet contains a COVID virus test or status, test, or phrase as a humorous opinion of COVID that does not refer to a personal experience.	"If you're on your own the same to, don't think you're there!"
Warning	Tweet contains an advertisement for an anti-viral product or service.	"Buy Anti-viral C to protect it by order (https://bit.ly/2H88L33)"
Open	Tweet is unrelated to COVID.	"Investment 400 (Investment) from Upper Publics: up 2 (2020) with a 100% return (100%) in 100% of cases!"

²⁵C Chew, G Eysenbach, *PloS one*, 2010

Multi-level classification of tweets ²⁶



²⁶DA Broniatowski, MJ Paul, M Dredze, *PLoS one*, 2013

Even finer distinctions ²⁷

- Infection vs concerned awareness.
going over to a friends house to check on her son. he has the flu and i am worried about him
starting to get worried about swine flu...
- Self vs other
- Part of speech templates constructed from word class features

Class Name	Words in Class
Infection	getting, got, recovered, have, having, had, has, catching, catch, cured, infected
Possession	bird, the flu, flu, sick, epidemic
Concern	afraid, worried, scared, fear, worry, nervous, dread, dreaded, terrified
Vaccination	vaccine, vaccines, shot, shots, mist, tamiflu, jab, nasal spray
Past Tense	was, did, had, got, were, or verb with the suffix "ed"
Present Tense	is, am, are, have, has, or verb with the suffix "ing"
Self	I, I've, I'd, I'm, im, my
Others	your, everyone, you, it, its, u, her, he, she, he's, she's, she, they, you're, she'll, he'll, husband, wife, brother, sister, your, people, kid, kids, children, son, daughter

²⁷A Lamb, MJ Paul, M Dredze, *HLT-NAACL*, 2013

The SIRS equations are given by:

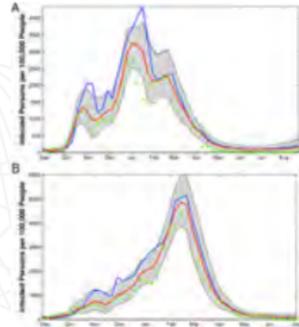
$$\begin{aligned}\frac{dS}{dt} &= \frac{N-S-I}{L} - \frac{\beta(t)SI}{N} - \alpha \\ \frac{dI}{dt} &= \frac{\beta(t)SI}{N} - \frac{I}{D} + \alpha\end{aligned}\quad (2)$$

where the AH modulated reproductive number is given by

$$R_0(t) = \exp(a \times q(t) + b) + R_{0min} \quad (3)$$

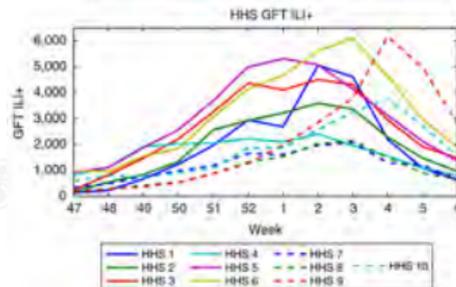
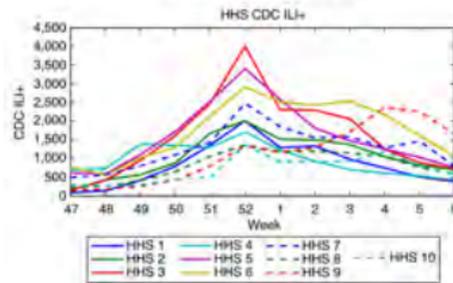
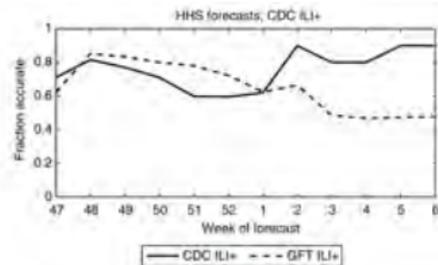
where, $a = -180$ and $b = \log(R_{0max} - R_{0min})$. $q(t)$ is the time varying specific humidity.

- GFT ILI estimates are assimilated to generate a posterior estimate of infection rates
- Captures long rise and single peak of infection during 2007–2008 as well as multiple modes during 2004–2005



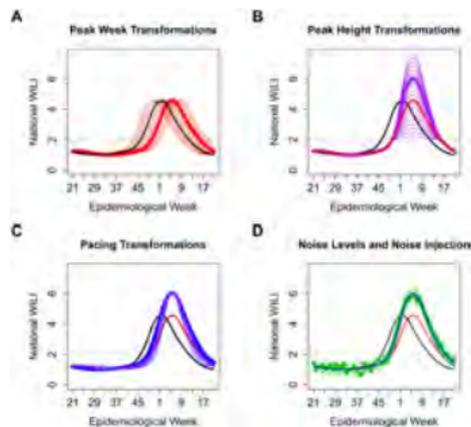
²⁸J Shaman, A Karspeck, *PNAS*, 2012

- First example of real-time forecasting
- Evaluated peak timing and peak value prediction
- By week 52, prior to peak for majority of cities, 63% of forecasts were accurate



²⁹J Shaman, A Karspeck, W Yang, J Tamerius, M Lipsitch, *Nat. Comm.*, 2013

- Performance comparison of different Kalman and Particle Filters.
- Geographical considerations (Hong Kong)
- Empirical Bayes Framework: improves flexibility of modeling.

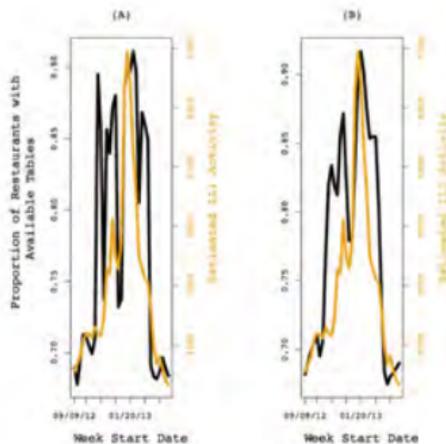


³⁰W Yang, A Karspeck, J Shaman, *PLOS Comp. Biol.*, 2015

³¹W Yang, BJ Cowling, EHY Lau, J Shaman, *PLOS Comp. Biol.*, 2015

³²LC Brooks, DC Farrow, S Hyun, RJ Tibshirani, R Rosenfield, *PLOS Comp. Biol.*, 2015

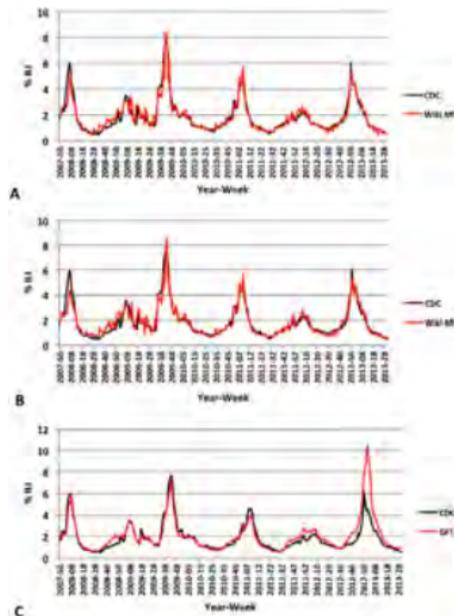
- Daily search performed for restaurants with available tables for 2 at the hour and half past the hour for 22 distinct times: between 11am–3:30pm and 6pm–11:30pm
- Multiple cities in US and Mexico



³³EO Nsoesie, DL Buckeridge, JS Brownstein, *Online Journal of Public Health Informatics*, 2013

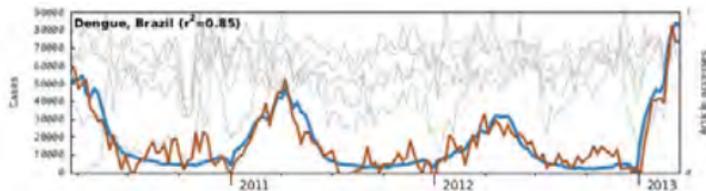
Monitoring Wikipedia usage ³⁴

- Handful of pages were identified and tracked for daily article view data
- LASSO model gives comparable performance to a full model



³⁴DJ McIver, JS Brownstein, *PLoS Computational Biology*, 2014

- Cholera, Dengue, Ebola, HIV/AIDS, Influenza, Plague, Tuberculosis
- Haiti, Brazil, Thailand, Uganda, China, Japan, Poland, Norway, US



- Reasons it doesn't work: noise, too slow, or too fast disease incidence

³⁵N Generous, G Fairchild, A Deshpande, SY Del Vallem, R Preidhorsky, *arXiv preprint*, 2014

Parking lot imagery

Estimating
“fill rate”
in parking lots

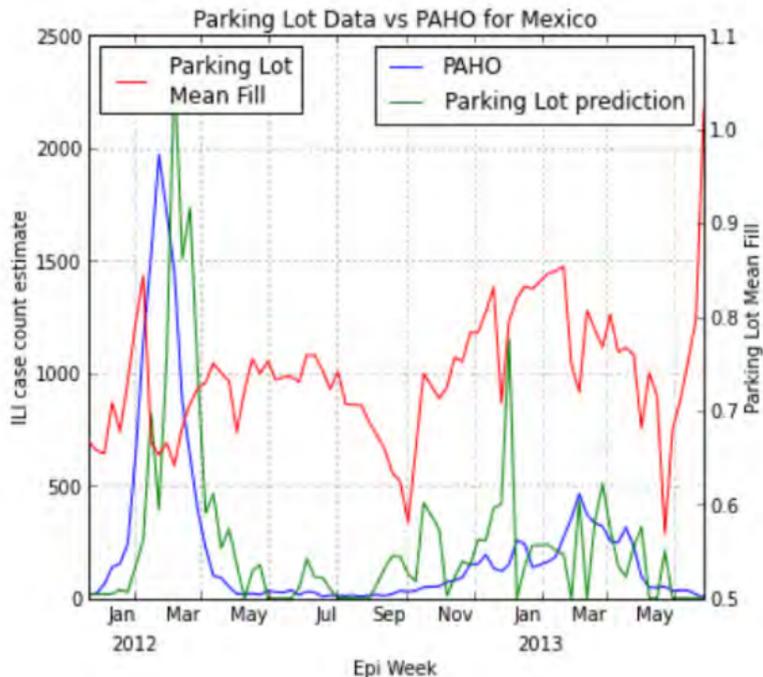


Hospital parking lot study in Latin America

<i>Country</i>	<i>Images Ordered</i>	<i>Images Used</i>	<i>Time Period</i>
Argentina	327	231	11/1/2011–5/26/2013
Mexico	1,566	781	11/1/2011–5/26/2013
Chile	682	292	11/1/2011–5/26/2013

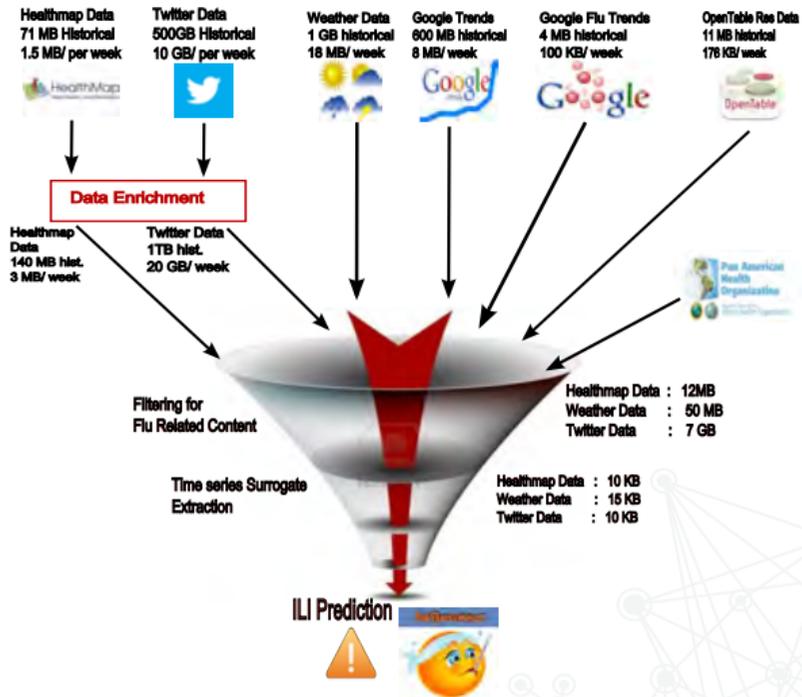


Parking lot imagery results ³⁶



³⁶P. Butler, N. Ramakrishnan, E. Nsoesie, J. Brownstein, *IEEE Computer*, 2014.

Putting it all together ³⁷



³⁷P Chakraborty, P Khadivi, B Lewis, A Mahendiran, J Chen, P Butler, EO Nsoesie, SR Mekaru, JS Brownstein, M Marathe, N Ramakrishnan, *SDM*, 2014

Putting it all together - contd (1)

Issues to consider

- How to combine different data sources: Model level fusion vs. data level fusion?
- How to accounting for initial, unreliable, estimates of official flu case counts
- Relationship between final flu counts and associated data sources is non-linear: How to get robust non-linear methods?
- Each data source (\mathcal{X}) represented as a multivariate weekly time-series with flu counts (P) as target variable - heavily skewed matrix and hence regression problem ill-defined

Putting it all together - contd (2)

Problem framework and solution sketches

- Solution (MFN): Matrix Factorization (dim reduction) + nearest neighbor search (non-linear) - similar to recommender systems ³⁸

- Data-Target Matrix $M = [XP]$

- Model

$$\widehat{\mathcal{M}}_{i,j} = \underbrace{b_{i,j}}_{\text{avg. value}} + \underbrace{U_i^T F_j}_{\text{dense subspace}} + \underbrace{F_j |\mathcal{N}(i)|^{-\frac{1}{2}} \sum_{k \in \mathcal{N}(i)} (\mathcal{M}_{i,k} - b_{i,k}) x_k}_{\text{weighted nearest neighbor}} \quad (4)$$

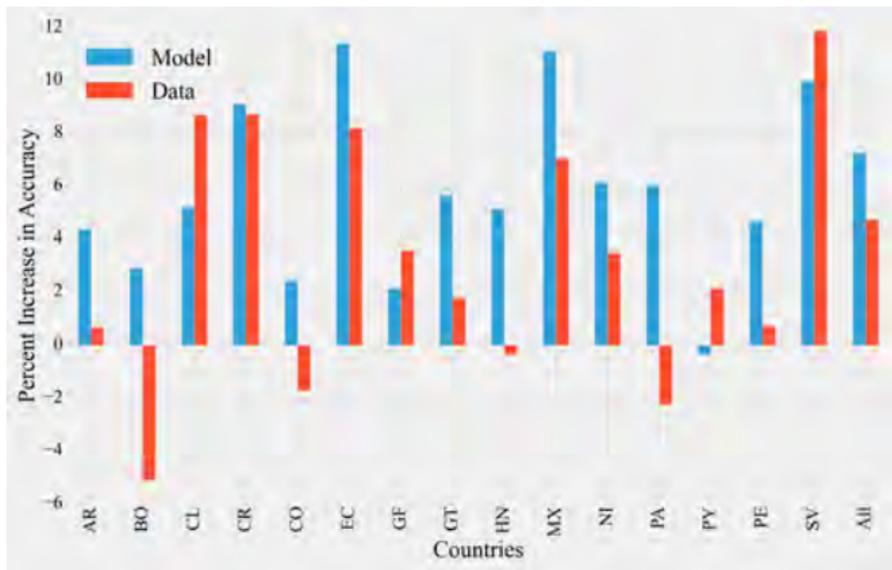
- Fitting

$$b_*, F, U, x_* = \underset{\text{loss on target variable}}{\operatorname{argmin}} \left(\sum_{i=1}^{m-1} \left(\mathcal{M}_{i,n} - \widehat{\mathcal{M}}_{i,n} \right)^2 \right) + \underbrace{\lambda_2 \left(\sum_{j=1}^n b_j^2 + \sum_{i=1}^{m-1} \|U_i\|^2 + \sum_{j=1}^n \|F_j\|^2 + \sum_k \|x_k\|^2 \right)}_{\text{L2 regularization on parameters}} \quad (5)$$

³⁸Y. Koren, KDD 2008

Putting it all together - contd (3)

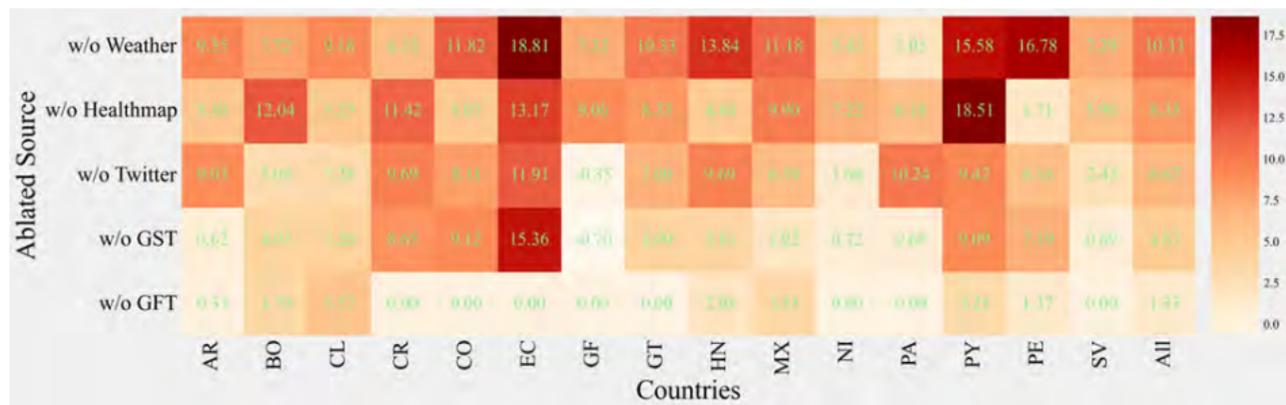
Model level (*MFN* with all data sets as \mathcal{X} vs. Source level (Two level *MFN* on each data source + output of data source)



- Model level involves lower computational complexity.
- Model level fusion on avg. produces more accurate forecasts.

Putting it all together - contd (4)

Which sources are most important?



- Weather sources appear to contribute most to performance gains.
- Importance of sources such as Twitter can also be seen - able to capture changes from baseline.

Putting it all together - contd (5)

Advantages of *MFN*

- Theoretical properties: Handles non-linearity and sparsity in a well defined framework. ³⁹
- Targeted: Custom non-linear and sparse methods allows for better reconstruction of target variables, sacrificing accuracy for non-target variables.
- Flexible: Easy to add different data sources and evaluate importance of each source via ablation.

Disadvantage

- Order of factorization needs to be found empirically
- Model is static - doesn't update over time
- reliable forecasting horizon is short

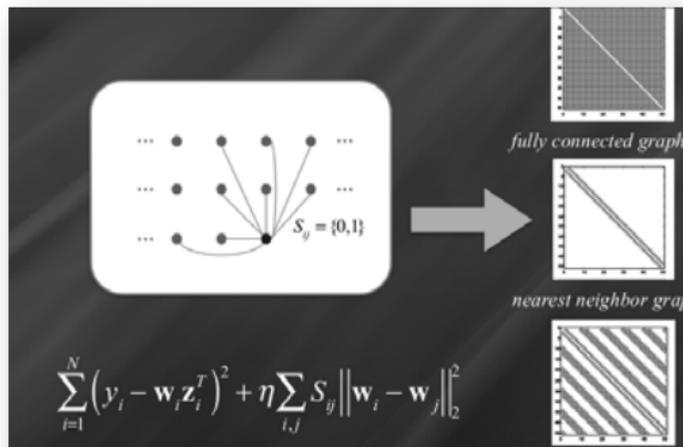
³⁹Y. Koren, KDD 2008



- Dynamic Model

$$y_i = \mathbf{w}_i \mathbf{z}_i^T + \varepsilon_i$$

- Similarity Constraints on time points



⁴⁰Z Wang, P Chakraborty, SR Mekaru, JS Brownstein, J Ye, N Ramakrishnan, *KDD*, 2015

Extending Forecasting Boundary - contd

- Dynamic GLMs to account for local variations.
- DARX: Identity Link

$$\sum_{i=1}^N (y_i - \mathbf{w}_i \mathbf{z}_i^T)^2 + \eta \sum_{i,j} S_{ij} \|\mathbf{w}_i - \mathbf{w}_j\|_2^2$$

- DPARX: Poisson Link

$$\min_{\mathbf{w}} \sum_i (\mathbf{w}_i \mathbf{z}_i^T - y_i \log(\mathbf{w}_i \mathbf{z}_i^T)) + \eta \sum_{i,j} S_{ij} \|\mathbf{w}_i - \mathbf{w}_j\|_2^2$$

s.t. $\mathbf{w}_i \mathbf{z}_i^T \geq 0, \forall i.$

Step	Method	AR	BO	CL	MX	PE	PY	US
1	ARX	2.85	2.63	3.18	2.61	2.51	2.82	3.71
	MFN	2.33	2.41	2.34	2.69	2.48	2.54	3.73
	SARX	3.02	2.42	3.11	2.90	2.81	2.69	3.67
	DARX	3.05	2.74	3.12	2.78	2.50	2.65	3.71
	DPARX	3.13	2.82	3.18	2.97	2.64	2.81	3.72
2	ARX	2.38	2.22	2.83	1.88	1.90	2.57	3.47
	MFN	2.12	2.00	2.13	2.33	2.21	2.19	3.63
	SARX	2.75	2.03	2.76	2.64	2.43	2.43	3.64
	DARX	2.94	2.68	3.02	2.58	2.38	2.58	3.60
	DPARX	2.86	2.70	2.89	2.64	2.52	2.65	3.61
3	ARX	2.11	1.86	2.61	1.28	1.44	2.31	3.19
	MFN	1.99	1.87	2.11	2.14	2.10	2.09	3.33
	SARX	2.33	1.61	2.46	2.42	2.16	2.23	3.40
	DARX	2.66	2.36	2.77	2.37	2.26	2.46	3.41
	DPARX	2.58	2.54	2.56	2.45	2.37	2.52	3.42
4	ARX	1.84	1.61	2.39	0.88	1.12	2.22	2.92
	MFN	1.85	1.81	2.00	2.05	2.01	1.94	3.15
	SARX	2.12	1.41	2.30	2.22	2.02	2.09	3.30
	DARX	2.34	2.21	2.52	1.98	2.19	2.22	3.18
	DPARX	2.29	2.35	2.32	2.26	2.20	2.40	3.20

DPARX performs better overall.

Recommendations for future forecasting programs ⁴¹

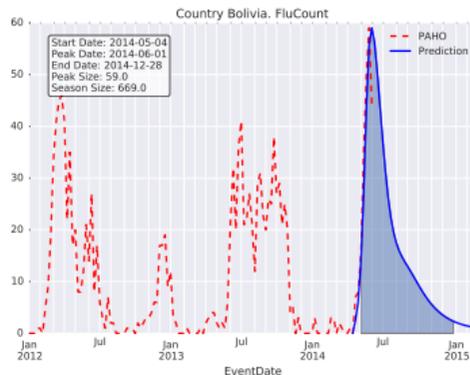
- Development of best practices for forecasting studies
- Head-to-head comparison of forecasting methods
- Assessment of model calibration
- Methods to incorporate subjective input into forecasting models
- Pilot studies to assess usefulness in real-world settings
- Improved mutual understanding between modelers and public health officials

⁴¹J Chretien, D George, E McKenzie *Online Journal of Public Health Informatics*, 2014

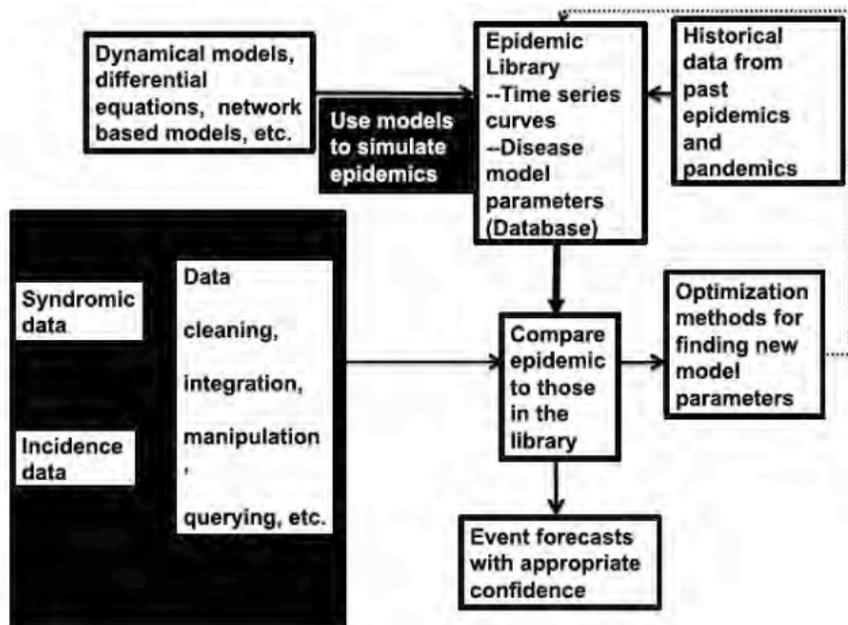
Epicurve Forecasting

Provide more actionable information for public health surveillance

- Start of season
- End of season
- Peak time
- Peak number of infections
- Total number of infections



Simulation Optimization Approach



Simulation Optimization Approach - more details

■ Parameters

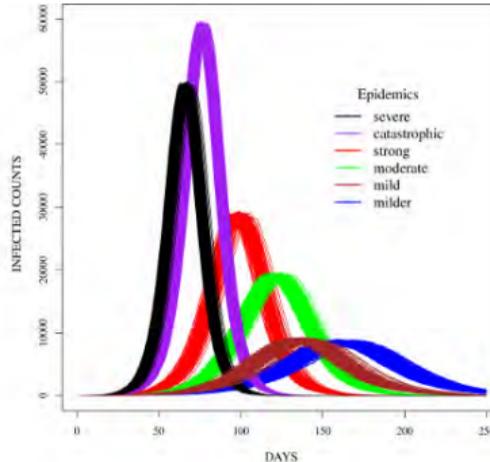
- 1** Transmissibility: The rate at which disease propagates through propagation
- 2** Incubation period: Duration between infection and onset of symptoms
- 3** Infectious period: Period during which infected persons shed the virus

■ Typical strategy

- 1** Seed a simulation (e.g., with simulated ILI count or with GFT data)
- 2** Use a direct search parameter optimization algorithm (Nelder-Mead, Robbins-Monro) to find parameter sets
- 3** Use the discovered parameter sets to forecast for next time frame (e.g., week)
- 4** Repeat for the whole season

Classifying epidemic curves ⁴²

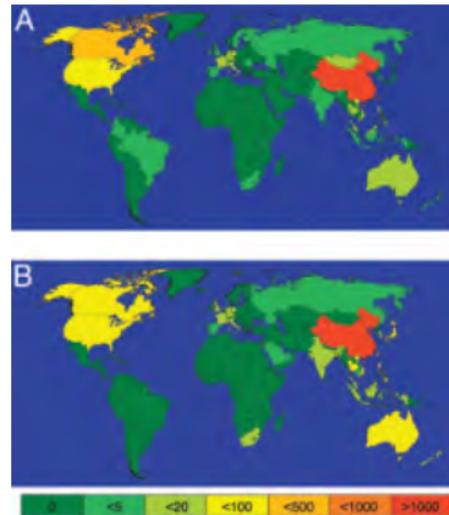
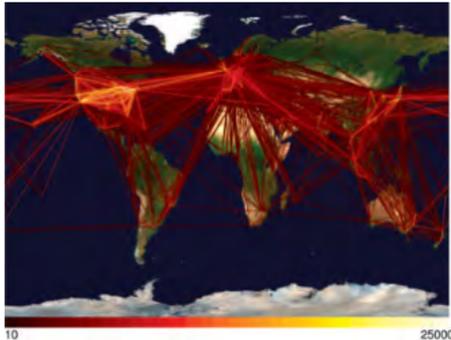
- Dirichlet process model to classify epidemic curves
- CRP representation of Dirichlet process model enabled classification into (Normal, Poisson, Negative Binomial)



⁴²EO Nsoesie, SC Leman, MV Marathe, *BMC infectious Dis.*, 2014

Forecasting Global Epidemic Spread ⁴³

- Uses aviation data to define a weighted network between airports
- Aims to replicate the global spread of SARS
- Stochastic SIR model to capture fluctuations



⁴³L. Hufnagel, D. Brockmann, T. Geisel, *PNAS*, 2004

Mapping interactions using Twitter ⁴⁴

- Latent variable modeling to capture interactions between people solely through their Twitter status updates
- 51,000 individuals traveling between 100 airports in 75 cities
- 73,460 flights inferred and 445,812 meetings inferred from Twitter updates
- Goal was to explain variation in flu incidence across cities
 - 1 Raw airline traffic volume: 56%
 - 2 Health of individual passengers: 17%
 - 3 Physical encounters between healthy and sick individuals: 5%



⁴⁴S Brennan, A Sadilek, H Kautz, *IJCAI*, 2013

A sobering study

Smallpox simulation under human mobility assumptions ⁴⁵

- Intentional release can have global effects
- Outbreaks can spread to different continents even before detection
- Outbreaks can happen in countries without necessary health infrastructure



Early detection + targeted vaccination suffices over mass vaccination ⁴⁶

⁴⁵B Goncalvez, D Balcan, A Vespignani, *Nature Scientific Reports*, 2013

⁴⁶S. Eubank et al., *Nature*, 2004.

Some Notable Mentions

- Exploring novel data streams to enhance disease surveillance ⁴⁷.
- Spatio-temporal modeling of 2014 Ebola outbreak ⁴⁸
- Individualizing prediction of Disease Trajectories ⁴⁹.

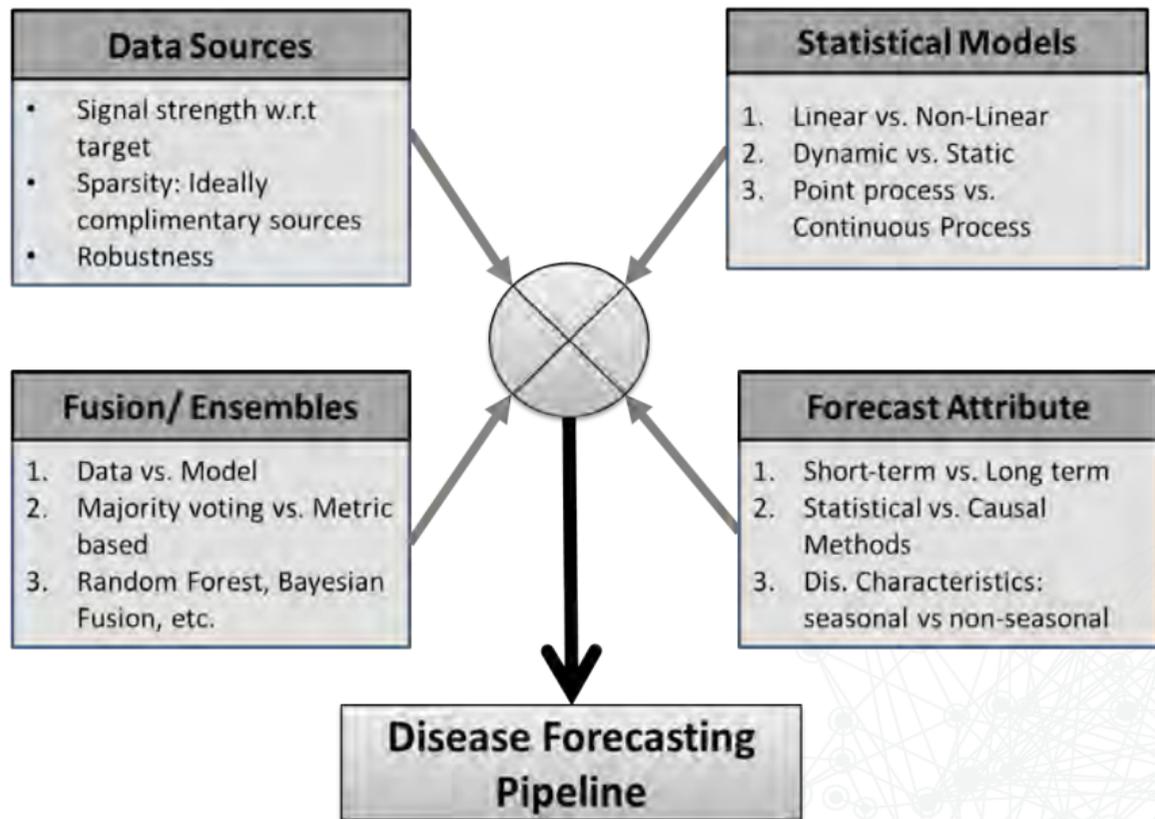
⁴⁷BA Althouse et al., *EPJ Data Science*, 2015

⁴⁸S Merler et al., *The Lancet Infectious Diseases*, 2015

⁴⁹P Schulam, S Saria, *NIPS*, 2015



Rounding Up: The Big Picture



Disease Forecasting Competitions

- IARPA Open Source Indicator Program. ⁵¹, 2010-2014
- CDC Influenza Prediction Challenge, 2013-current
- DARPA Chikungunya Prediction Challenge, 2014
- RAPIDD Ebola Challenge, 2015

⁵¹EMBERS, <http://dac.cs.vt.edu/research-project/embers/>



- 1 Goals, History, Basic Concepts
- 2 Dynamics and Analysis
- 3 Surveillance and Forecasting
- 4 Control and optimization**
- 5 Putting it all together: theory to practice



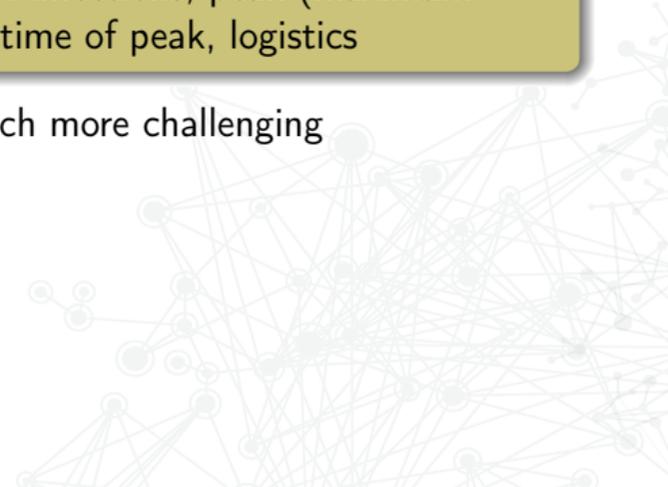
Controlling the spread of epidemics

General problem

Given a partially known network, initial conditions and disease model:

- Design interventions for controlling the spread of an epidemic
- Different objectives, such as: number of infections, peak (maximum number of infections at any time) and time of peak, logistics

Complement of influence maximization: much more challenging



Optimization Problems in GDS

Let $\mathcal{P}(\mathcal{S})$ denote the phase space of a given SyDS $\mathcal{S}(G)$. Modify \mathcal{S} optimally so that the set of reachable states in $\mathcal{P}(\mathcal{S})$ satisfies a given property.

- **Property \mathcal{P}_1 :** #1's in configuration is "small" \equiv interventions that try to minimize the outbreak size
 - Modify graph by removing nodes (vaccination) or edges (quarantining) so that fixed points in $\mathcal{P}(\mathcal{S})$ satisfy \mathcal{P}_1
- Similarly, reducing epidemic duration \equiv reducing transient length in $\mathcal{P}(\mathcal{S})$

GDS view: enables many algorithmic and complexity results to be translated across systems

Objectives and strategies for controlling epidemics

- Different objectives
 - Expected outbreak size
 - In the whole population and in different subpopulations
 - Other economic costs
 - Duration of epidemic
 - Size and time of peak
- Different kinds of strategies⁵²
 - Decrease β , the transmissibility
 - Quarantining and social distancing of infected individuals
 - Hand washing and other hygienic precautions
 - Treating infected individuals with antimicrobials
 - Reduce number of susceptibles: vaccination
 - Reduce infectious duration: treatment with antimicrobials
 - Increase δ : culling animals
- Interventions can be modeled in networks as node deletions (vaccination), edge deletion (quarantining) and reducing β on edges

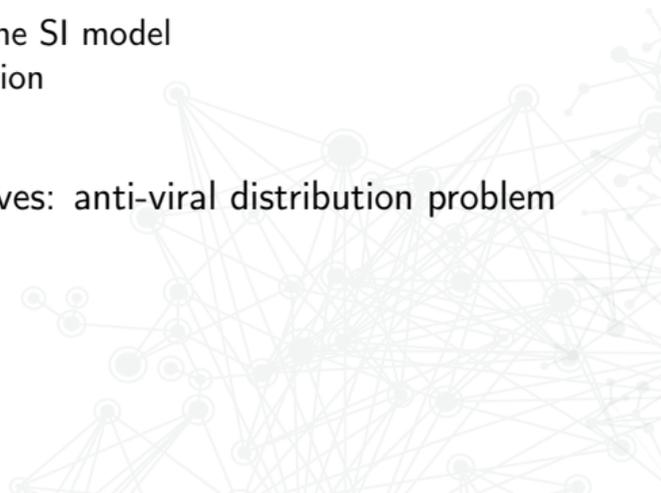
⁵²Dimitrov and Meyers, *INFORMS*, 2010

Different kinds of issues in studying interventions as optimization problems

- Resource constraints, e.g., budget for vaccines to use
- Complex and multiple objective functions, e.g., expected outbreak size, peak size and duration
 - Need multi-criteria optimization
- Implementability and compliance
 - Interventions should be described succinctly
- Individual utility: game-theoretical issues
- Computationally very hard problems
 - Computing basic properties related to epidemics (e.g., probability that a node gets infected) is $\#P$ -hard in network models
 - Optimization problems NP-hard even for very simplistic settings (e.g., SI model or simple contagion)
 - Metaheuristics do not give any insights into how well they perform (relative to the best possible).

Outline for this section

- Centralized interventions: minimizing social cost
 - Vaccine allocation problems in the SI model on arbitrary networks: bicriteria approximation algorithm
 - Vaccination strategies based on the spectral characterization in the SIS model: approximation algorithms
 - Optimal vaccination policies using ODE approach
- Vaccination games
 - Network based vaccination game in the SI model
 - Game based on spectral characterization
- Sequestration of critical populations
- Combining individual and social objectives: anti-viral distribution problem (discussed later)



Vaccination allocation problems

Optimal vaccine allocation problem (OVAP)

Given a graph G and limited supply of vaccine (B doses), how should it be allocated to different sub-populations so that different epidemic outcomes are optimized?

- Algorithm has approximation ratio α if for any instance \mathcal{I} of the problem, it finds a solution S such that $\text{cost}(S) \leq \alpha \cdot \text{cost}(OPT(\mathcal{I}))$
- Simplest setting: SIR model with transmission probability 1 (“highly contagious disease”)
 - NP-hard to approximate within factor of $O(n^\delta)$ for any $\delta < 1$
 - If initial infected set is given: bicriteria-approximation, which uses B/ϵ vaccines, so that #infections is at most $1/(1 - \epsilon)$ times optimal^{53 54}
 - If initial infection is random: $O(\log n)$ approximation⁵⁵

⁵³A. Hayrapetyan, D. Kempe, M. Pal and Z. Svitkina, *ESA*, 2005

⁵⁴S. Eubank, V. S. Anil Kumar, M. Marathe, A. Srinivasan and N. Wang, *AMS DIMACS*, 2005

⁵⁵V. S. Anil Kumar, R. Rajaraman, Z. Sun and R. Sundaram, *IEEE ICDCS*, 2010

Controlling epidemics in the SIS model

- Reduce spectral radius below T to ensure the epidemic dies out fast.
- Spectral radius can be reduced by deleting nodes (vaccination) or edges (social distancing)

Spectral Radius Minimization (SRM) problem

- *Given:* graph $G=(V, E)$, threshold T and cost $c(e)$ for edges
- *Objective:* choose cheapest set $E' \subseteq E$ of edges to delete, so that $\lambda_1(G[E - E']) \leq T$.

Similarly: node version

Reducing the spectral radius to control epidemic spread

- Interventions (node/edge deletion) to reduce spectral radius below given threshold
- NP-hard to approximate within a constant factor
- Heuristics based on components of the first eigenvector and degree: [Tong et al., 2012], [Van Mieghem et al., 2011]
- Node version: if G has a power law degree sequence with exponent $\beta > 2$ and $T^2 \leq cd_{max}$, then a high degree strategy gives an $O(T^{\beta-1})$ approximation ([S. Saha, A. Adiga and A. Vullikanti, AAAI 2014])
- Node version: $\Theta(1)$ approximation by a high degree strategy in Chung-Lu random graphs with power law weights with exponent $\beta > 2$.

Compartmental differential equation based approach for OVAP⁵⁹

- Age-structured differential equation model for H1N1
 - Mixing between age groups based on survey data⁵⁶
 - $R_0 = 1.4$ for swine flu⁵⁷
 - Different outcomes: deaths, infections, years of life lost, contingent valuation, and economic costs
 - Mortality considerations based on 1957 and 1918 pandemics
 - Valuations and economic costs of sickness and death from health economics literature⁵⁸
- CDC guidelines for swine-flu: prioritize vaccination for children 6 months to 5 years, and 5-18 years

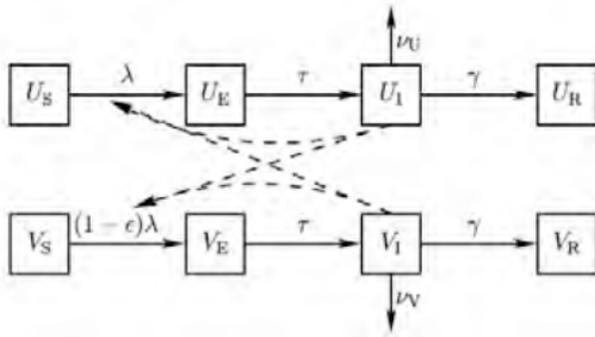
⁵⁶J. Mossong et al., *PLoS Med.*, 2008

⁵⁷C. Fraser et al., *Science*, 2009

⁵⁸Such as: A. C. Haddix et al., *Oxford University Press*, 1996; M. Meltzer et al., *Emerg. Infect. Dis.*, 1999

⁵⁹Medlock and Galvani, *Science*, 2009

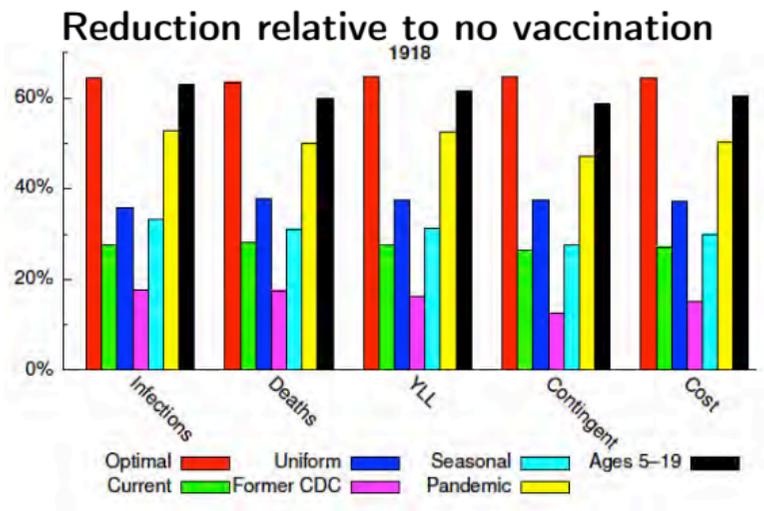
Coupled differential equation model



$$\begin{aligned} \frac{dU_{S_a}}{dt} &= -\lambda_a U_{S_a} \\ \frac{dU_{E_a}}{dt} &= \lambda_a U_{S_a} - \tau_a U_{E_a} \\ \frac{dU_{I_a}}{dt} &= \tau_a U_{E_a} - (\gamma_{U_a} + \nu_{U_a}) U_{I_a} \\ \frac{dU_{R_a}}{dt} &= \gamma_{U_a} U_{I_a} \\ \frac{dV_{S_a}}{dt} &= -(1 - \epsilon_a) \lambda_a V_{S_a} \\ \frac{dV_{E_a}}{dt} &= (1 - \epsilon_a) \lambda_a V_{S_a} - \tau_a V_{E_a} \\ \frac{dV_{I_a}}{dt} &= \tau_a V_{E_a} - (\gamma_{V_a} + \nu_{V_a}) V_{I_a} \\ \frac{dV_{R_a}}{dt} &= \gamma_{V_a} V_{I_a} \end{aligned}$$

- 17 different age classes, indexed by a
- $U_{S_a}(t), U_{E_a}(t), U_{I_a}(t), U_{R_a}(t)$: number of unvaccinated susceptible, latent, infectious and recovered
- $V_{S_a}(t), V_{E_a}(t), V_{I_a}(t), V_{R_a}(t)$: number of vaccinated susceptible, latent, infectious and recovered
- Vaccine allocation: $\sum_a V_{S_a}(t) + V_{E_a}(t) + V_{I_a}(t) + V_{R_a}(t)$

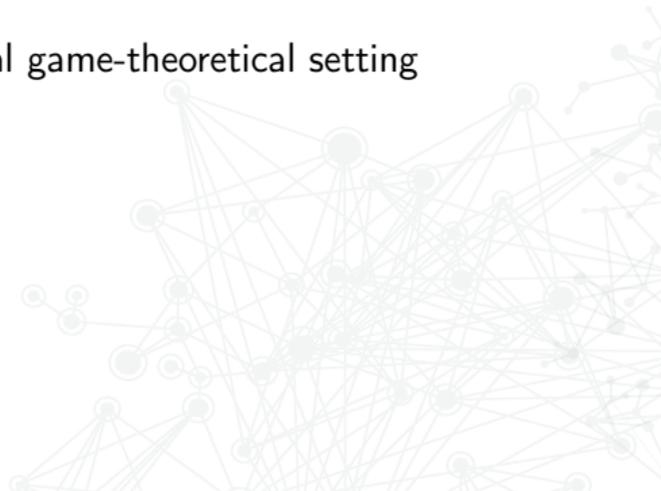
Results



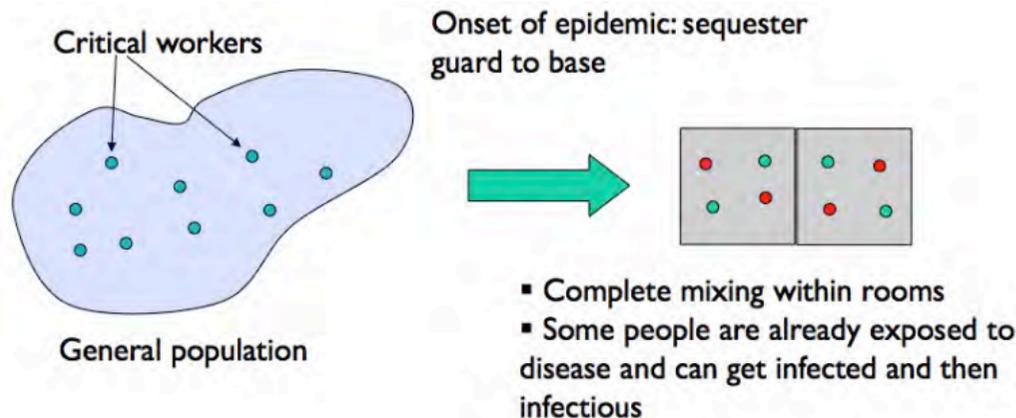
- Optimal allocation to different age groups depends on the objective and the number of available doses
- Significantly better than CDC guidelines at that time, allocation to age group 30-39
- High sensitivity to disease model and other parameters

Decentralized vaccination decisions

- Vaccination or other interventions leads to cost (say C) for an individual
- Infection cost L (typically higher than C)
- *Herd immunity*: if enough neighbors get vaccinated, then low probability of infection
- Individual utility for vaccination: natural game-theoretical setting



Sequestration for protecting critical sub-populations

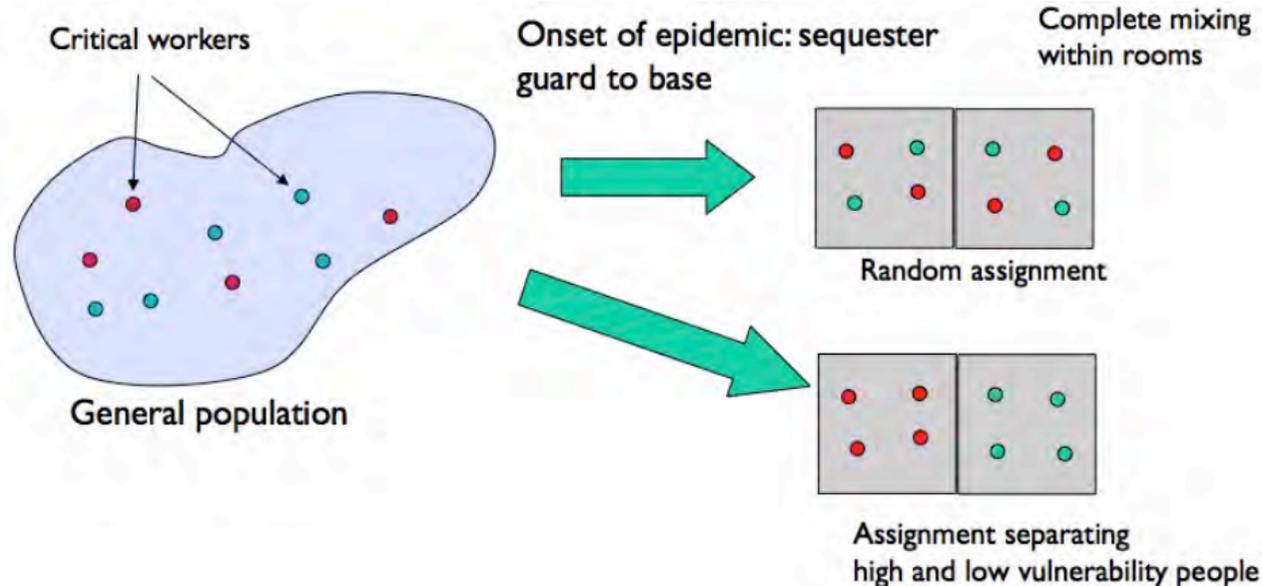


Goal

Partition people into groups so that overall outbreak is minimized

- 1918 epidemic: thought to have spread primarily through military camps in Europe and USA
- Large outbreaks in naval ships

Sequestration problem



- Cannot do much without any information about the individuals
- Assume estimates $f(i)$ of vulnerability: probability the node i gets infected (for some initial conditions)

Sequestration problem

Sequestration Problem

Given: a set V of people to be sequestered in a base, group size m , number of groups k and vulnerability $f(i)$ for each $i \in V$.

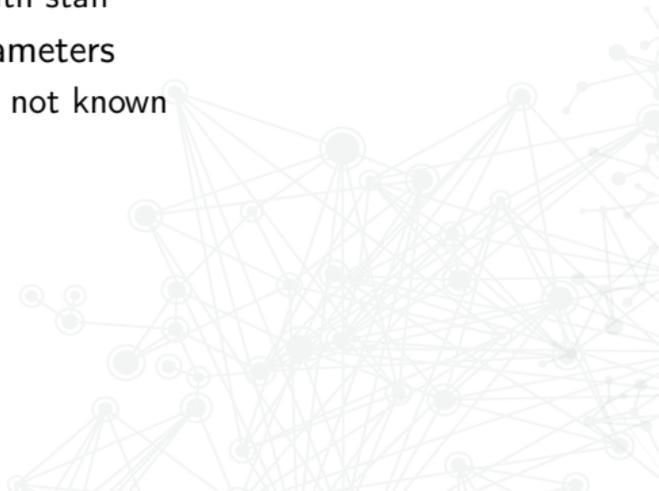
Objective: partition V into groups V_1, V_2, \dots, V_k so that the expected number of infections is minimized.

- Assume complete mixing within each group with transmission probability p among any pair of nodes
 - Individual i is (externally) infected with probability $f(i)$. Additionally, the disease can spread within each group, following an SIR process.
-
- Efficient exact algorithm for group sequestration⁶⁰
 - Significantly outperforms random allocation

⁶⁰C. Barrett et al., *ACM SIGHIT International Health Informatics Symposium*, 2012

Research challenges

- Need to find implementable strategies
 - Identifiable attributes such as: demographics, geographical locations
 - Temporal strategies: Markov Decision Processes
- Complex objectives and constraints
 - Logistics of production and delivery of medicines
 - Economies of scale
 - Resource constraints, e.g., public health staff
- Uncertainty in network and disease parameters
 - Network, state and model parameters not known
 - Multiple and evolving disease strains
- Compliance and behavioral changes
 - Network co-evolves with epidemic



- 1 Goals, History, Basic Concepts
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- 5 Putting it all together: theory to practice**



Putting it all together: outline

- Recent real-world examples: 2009 H1N1 and 2014-15 Ebola Outbreak
- Data, Synthetic realistic social networks
- Detailed agent-based simulations
- Case studies
- Computational Ecosystems
- Extensions



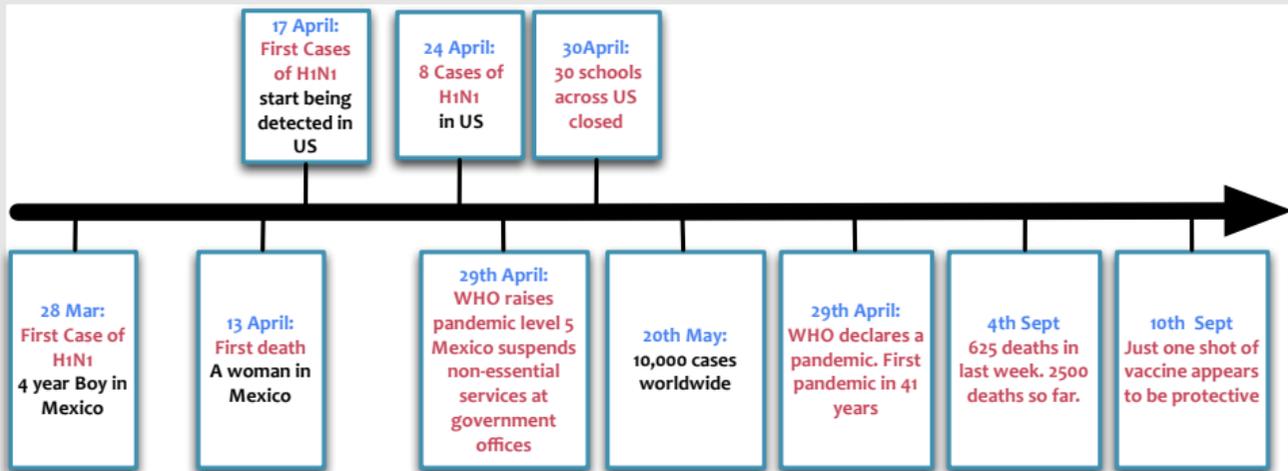
Supporting outbreak response and preparedness exercises



Unfolding of a pandemic

Timeline: http://www.nbcnews.com/id/30624302/ns/health-cold_and_flu/t/timeline-swine-flu-outbreak/#.U_LBJUgdXxs

Timeline for H1N1



Pandemic Influenza Planning

Problem

How can we prepare for a likely influenza pandemic?

Study Design

Population: Chicago Metropolitan area, 8.8 million individuals

Disease: Pandemic Influenza, R0 1.9, 2.4, and 3.0, varying proportion symptomatic

Interventions: Social distancing, School closure, and prophylactic anti-virals triggered when 0.01%, 0.1%, and 1% of population is infected

Modeling tool

EpiSims manually configured to 6 different scenarios specified by decision-maker

Policy recommendations

Non-pharmaceutical interventions can be very effective at moderate levels of compliance if implemented early enough



Fall 2006

2006

Antiviral Distribution Planning

Problem

What is the impact of encouraging the private stockpiling of antiviral medications on an Influenza pandemic?

Study Design

Population: Chicago Metropolitan area, 8.8 million individuals

Disease: Pandemic Influenza, calibrated to 33% total attack rate

Parameter of interest: Different methods of antiviral distribution (private insurance-based, private income-based, public, random)

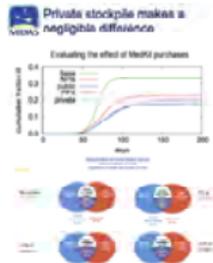
Other parameters: Percent taking antivirals, Positive predictive value of influenza diagnosis, School closures, Isolation

Modeling tool

EpiFast, specifically modified for this study and manually configured to explore multiple parameter interactions and sensitivities

Policy recommendations

Private stockpiling of antiviral medications has a negligible impact on the spread of the epidemic and merely reduces demands on the public stockpile.



Summer 2007

2009

Emergence of H1N1 Influenza

Problem

What are the characteristics of this novel H1N1 influenza strain and their likely impact on US populations?

Study Design

Population: Various metropolitan areas throughout the US

Disease: Novel H1N1 Influenza

Parameters Studied:

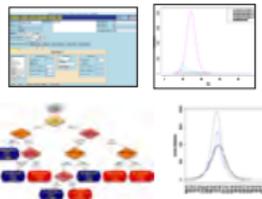
- Levels and timing of Social Distancing, School Closure, and Work Closure
- Viral mutation causing diminished immunity, seasonal increase in transmissibility, size of 2nd wave, timing of changes, reduced vaccine uptake

Modeling tool

Initial configurations with DIDACTIC, then manual configurations were made to web-enabled epidemic modeling and analysis environment based on EpiFast simulation engine

Policy recommendations

- The novel strain of H1N1 influenza presents a risk to becoming a pandemic, limited data make predicting exact disease characteristics difficult
- Several conditions would have to align to allow a sizeable 3rd wave to occur



Spring - Fall 2009

Adenovirus Pandemic Simulation and Analysis

Problem

How can decision makers become familiar with the challenges and decisions they are likely to encounter during a national pandemic, mainly centered on the allocation of scarce resources?

Study Design

Population: US (contiguous 48 states)

Disease: Adenovirus 12v

Interventions: None (request for unmitigated disease)

Other Details: Novel fusion of both coarse scale national level model and high resolution state-wide transmission to generate estimates of demand for scarce medical resources

Modeling Tool

National Model and EpiFast

Policy Recommendations

Nationwide epidemics of a severe respiratory illness will create complex demands on the medical infrastructure, which will require high-level coordination to maximize the delivery of care.



Summer 2013

2012

Recent example: Ebola outbreak in Africa

- Largest Ebola outbreak till date: 5 countries; 28000 cases; 10500 deaths (WHO, Sept 2015)



Recent example: Ebola outbreak in Africa

- Largest Ebola outbreak till date: 5 countries; 28000 cases; 10500 deaths (WHO, Sept 2015)
- Beautifully done NY Times webpage:
<http://www.nytimes.com/interactive/2014/07/31/world/africa/ebola-virus-outbreak-qa.html>

Important Questions

- 1 How many people have been infected?
- 2 Where is the outbreak?
- 3 How did it start; tracing the first few cases.
- 4 Chances of getting Ebola in the US?
- 5 How does this compare to past outbreaks?
- 6 How contagious is the virus? Why is Ebola so difficult to contain?
- 7 How does the disease progress? How is the disease treated?
- 8 Where does the disease come from?

NY Times Graphics



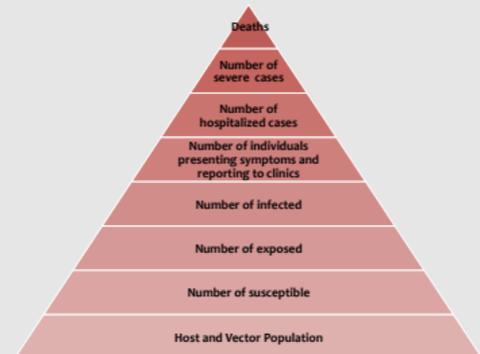
Details of the disease

- Started in a village near Gueckedou, Guinea,
- Natural reservoirs (fruit bats)
- Cultural practices, lack of strong public health infrastructure and lack of trust due in public officials due to long civil war all played a part.
- Human to human transmission: body fluids
- No effective vaccines, or anti-virals developed during the outbreak
- **Disease parameters:** (i) Average incubation period: approximately 12 days; (ii) Symptom onset to recovery/death: approximately 9 days; (iii) Overall case-fatality ratio: approximately 54%
- **What worked?:** Social interventions and boots on the ground public health response: Placement of Ebola treatment units (ETU); Personal protective equipment (PPE) for Healthcare workers; Improved surveillance and contact tracing; Community engagement - Safe burial practices
- Long term socio-economic and health impacts still being ascertained

Considerations

- Data is noisy, time lagged and incomplete
 - E.g. How many individuals are currently infected by Ebola?
- Policy is influenced not just by optimality of solutions but real-world considerations
- Good models are used as a part of evidence based decision making process

Epidemiology and Surveillance Pyramid



⁶¹Lipsitch et al., 2011, Van Kerkhove & Ferguson 2013, National Pandemic Influenza Plan

Questions our group worked on

- 1 Estimating basic epidemiological parameters
- 2 Forecasting the ongoing epidemic with & without control
- 3 Assessing the threat of imported cases in the US and Latin America causing secondary infections
- 4 Efficiently allocating potential pharmaceutical treatments
- 5 Location of Emergency treatment centers and assessing their impact
- 6 Estimating the need for supplies such as personal protective equipment
- 7 Analyzing social media for public mood & sentiments



AI in the real world

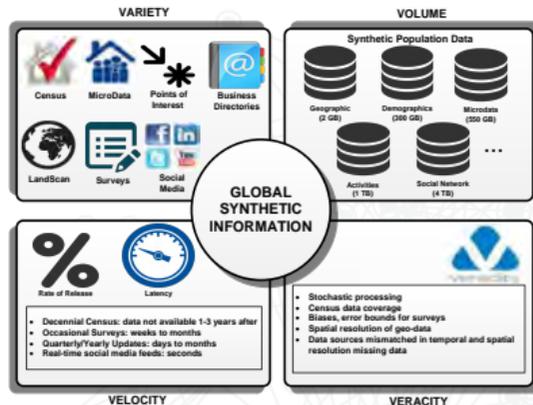
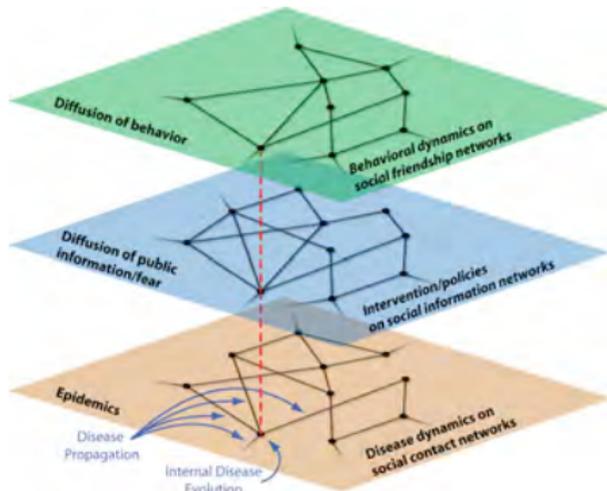


Elements of real-time computational epidemiology

- **Step 1.** Construct a synthetic realistic social contact network by integrating a variety of commercial and public sources.
- **Step 2.** Develop models of within-host disease progression using detailed case-based data and serological samples to establish disease parameters.
- **Step 3.** Develop high-performance computer simulations to study epidemic dynamics (exploring the Markov chain M).
- **Step 4.** Develop multitheory behavioral models and policies formulating and evaluating the efficacy of various intervention strategies and methods for situation assessment and epidemic forecasting. Use Markov decision processes to formulate and evaluate these policies.
- **Step 5.** Develop Cyber-ecosystems to support epidemiologists and policy makers for effective decision making.

Big data problem

- Synthesis of realistic networks
 - Data is noisy and time-lagged
 - Need new methods for information fusion and ML:
Currently using 34 databases
- Large complex networks
 - > 100GB input data: 300M people, 22B edges, 100M locations, 1.5B daily activities
 - Irregular network: Dimension reduction techniques (e.g. renormalization group techniques) do not apply
 - Coevolving behaviors and networks
- Large experimental design ⇒ multiple configurations



Step 1: Synthesizing Social Contact networks



Modeling social networks: random graph models

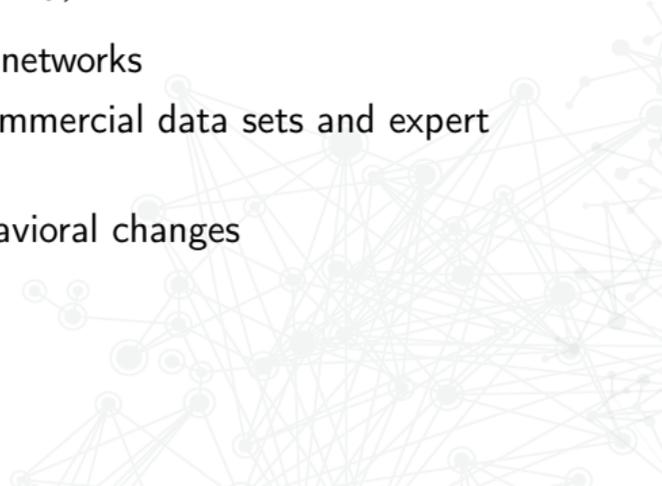
- *Erdős-Rényi* model, $G(n, p)$: Each edge $e = (u, v)$ is selected independently with probability p
- *Chung-Lu model*: given a weight sequence $\mathbf{w} = (w(v_1, V), w(v_2, V), \dots, w(v_n, V))$ for nodes $v_i \in V$, a random graph $G(\mathbf{w})$ is constructed as follows:
 - add each edge (v_j, v_k) independently with probability $\frac{w(v_j, V)w(v_k, V)}{\sum_{v_i \in V} w(v_i, V)}$
- Evolutionary models (e.g., preferential attachment): new node v connects to earlier nodes u with probability proportional to $deg(u)$
- Network models capture simple local properties, e.g., degree sequence, clustering coefficient
- Primary goal was to obtain analytical bounds
- Cannot model higher order properties, heterogeneities

Step 1: Synthesizing Social Contact networks

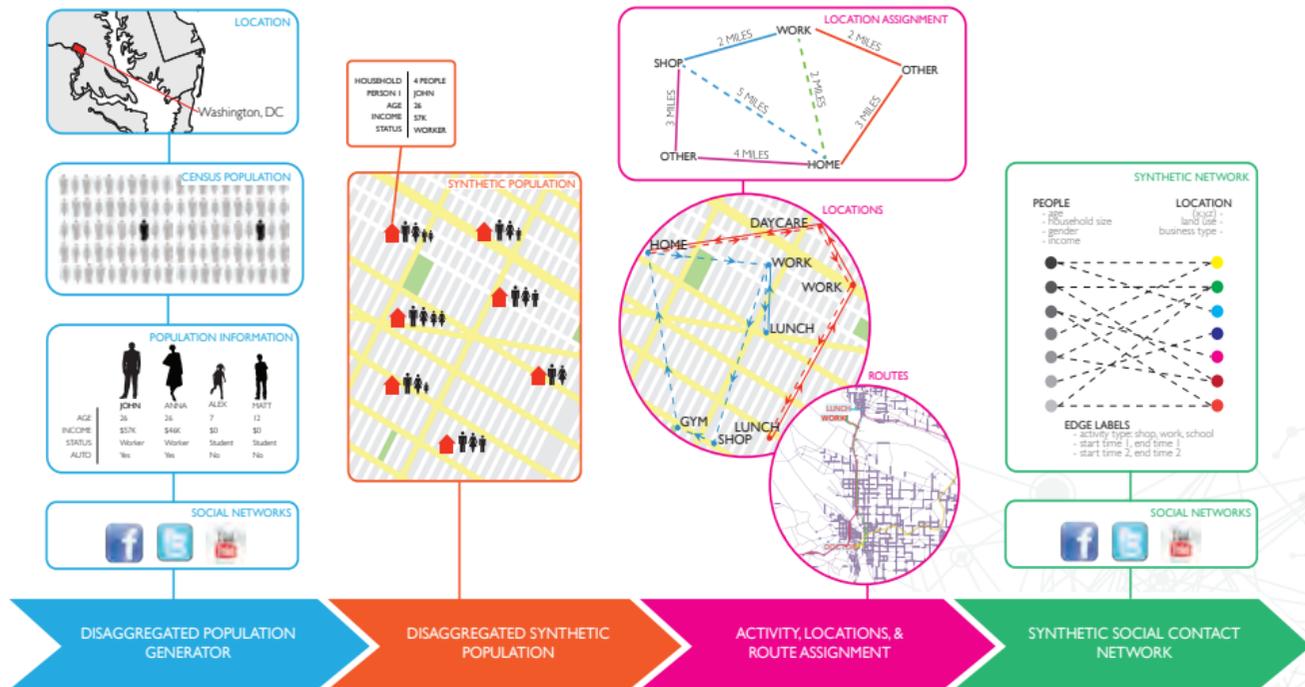


First principles based network synthesis

- For individuals in a population (representation of individuals):
 - Their demographics (Who)
 - The sequences of their activities (What)
 - The times of the activities (When)
 - The places where the activities are performed (Where)
 - The reasons for doing the activities (Why)
- No explicit data sets available for such networks
- Synthesis of a number of public and commercial data sets and expert knowledge
- Can explicitly model the impact of behavioral changes



A methodology for synthesizing social contact networks⁶²



⁶²Beckman et. al. 1995, Barrett et al. WSC, 2009, Eubank et al. Nature 2005, TRANSIMS project, 1997, 1999

Comparing various data collection techniques to infer mobility patterns⁶³

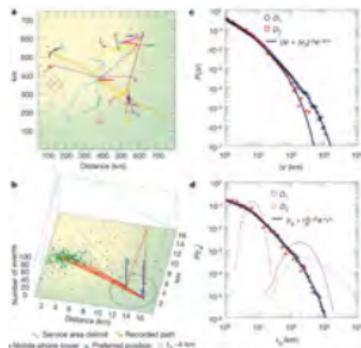
Methods	Advantages	Disadvantages
Survey & direct	Multi purposed use; fewer biases; can capture multiple correlations	can be expensive to collect data observations;
Wi-Fi localization	Accuracy; Energy usage 50% GPS	Providing access point is expensive
GPS localization	High spatial precision: 5m; Can distinguish between transportation modes	High battery (energy) usage; expensive; sampling biases; No (low quality) signal in indoor environment
Cellular network localization (passive) (Call Data Records);	Automatically generated;	Sparse in time; Lower spatial resolution (175m); Needs more filtering; sampling biases; Proprietary
Cellular network localization (active)	More accuracy than passive localization; Less expensive than previous methods	More costly than passive form; sampling biases; Proprietary and thus not publicly available

Characterizing human travel patterns using CDR ⁶⁵, ⁶⁶

100,000 Anonymized mobile phone users tracked for a 6-month period

$$P(\Delta r) = (\Delta r + \Delta r_0)^{-\beta} \exp(-\Delta r/\mathcal{K})$$

- Radius of gyration distribution rules out a traditional Levy flight distribution of step lengths



- Study by Lu et al. ⁶⁴ highlights that algorithms are capable of approaching the theoretical limits of predictability

⁶⁴X Lu, E Wetter, N Bharti, AJ Tatem, L Bengtsson, *Nature Scientific Reports*, 2013

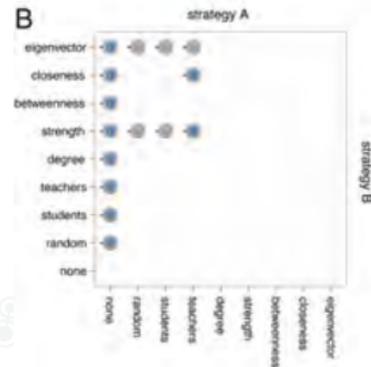
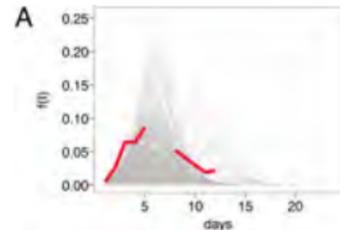
⁶⁵M Gonzalez, CA Hidalgo, A Barabasi, *Nature*, 2008

⁶⁶Becker et al, *CACM* 2013

Synthesizing social proximity networks using RFID tags and wifi localization^{67, 68}

Wireless sensor network motes distributed to students, teachers, staff at an American high school

- Social network reconstructed using 762,868 CPIs (close proximity interactions) at a maximal distance of 3 meters across 788 individuals
- Network exhibits typical small-world properties with high modularity
- SEIR model imposed over the network with 100 runs for each individual (78800 simulations)
- Secondary infections and R_0 in agreement with school absenteeism data during this period



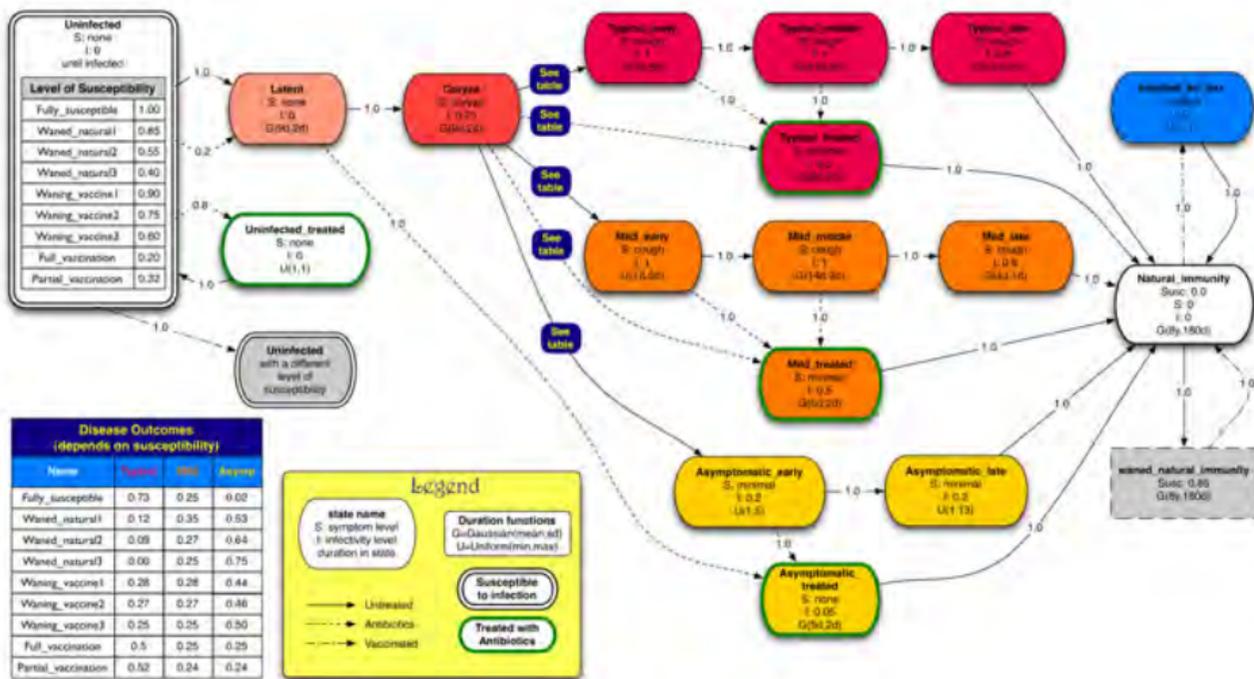
⁶⁷N Eagle, A Pentland, D Lazer, *PNAS*, 2009

⁶⁸M. Salathe et al., *PNAS*, 2010

Step 2: Within host disease progression models.



Within host disease progression model



- Parameter estimation is done using derivative free optimization method.
- Simulation based optimization approach

Step 3: Simulations to unravel the disease dynamics over a network



Computing epidemic dynamics over networks

- Recall: Theoretical results on computing dynamics for special classes of networks
- Worst case complexity: We are given an SIR GDS \mathcal{S} , an initial configuration \mathcal{I} and a final configuration \mathcal{B} . The goal is to decide whether \mathcal{S} starting from \mathcal{I} reaches \mathcal{B} with a non-zero probability or \mathcal{B} reaches with a probability $\geq \pi$ in $\leq t$ steps
- **Theorem** : For simple SIR GDS systems and for each $t \geq 3$, reachability in t time steps is **NP**-hard. It is **#P**-hard if we want to assure that \mathcal{B} reaches with a probability $\geq \pi$ Moreover, this result holds even when the initial configuration has one infected node

Implications: need to develop *fast simulations* to compute the epidemic dynamics in general

Fast high performance simulations: From 40 hours to 40 seconds

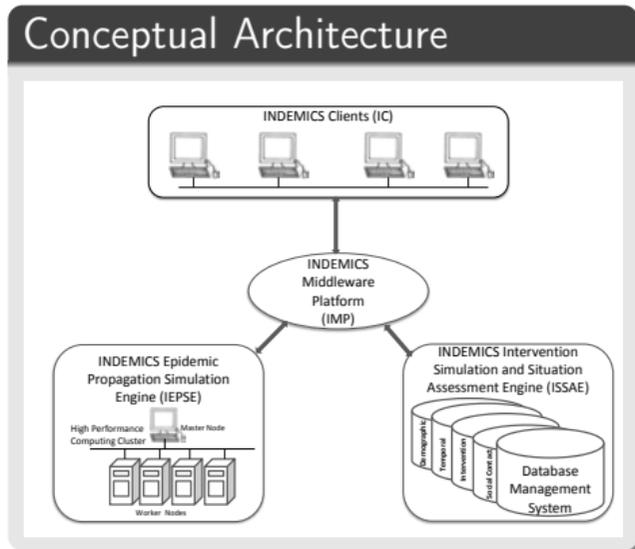
Distinguishing Features	EpiSims (Nature'04)	EpiSimdemics (SC'09,WSC'10)	EpiFast (ICS'09)	Indemics (ICS'10,TOMACS'11)
<i>Solution Method</i>	Discrete Event Simulation	Interaction-Based Simulation	Combinatorial +discrete time	Interaction-based, Interactive Simulations
<i>Performance 180 days 9M hosts & 40 proc.</i>	~40 hours	1 hour for 300Million nodes	~40 seconds	15min-1hour
<i>Co-evolving Social Network</i>	Can work	Works Well	Works only with restricted form	Very general
<i>Disease transmission model</i>	Edge as well as vertex based	Edge as well as vertex based (e.g. threshold functions)	Edge based, independence of infecting events	Edge based
<i>Query and Interventions</i>	restrictive	Scripted, groups allowed but not dynamic	Scripted and specific groups allowed	Very general: no restriction on groups

Simulating coevolving epidemics and interventions

- Computer experiments pertaining to control, resource allocation, planning in epidemiology are best viewed as a Markov decision process (MDP).
- Most simulations discussed in the literature have focused on disease progression; framing of interventions and their execution within a simulation is not well studied
- Epidemic analysis = disease spread + situation assessment + interventions
- Leads to separation of concerns: disease spread is best computed by interaction based methods, interventions are best specified as a (query, action) tuple.
- What is the best way to structure such modeling environments?
 - Need a natural language for representing (query, action) tuple
 - Need the ability for the simulation to start and stop
 - Typically, a public health analyst should be able to formulate a new intervention: they need not have to work with complex parallel code

Indemics

- Simulation can start and stop at any desired point
- Detailed state assessment (e.g. is Tom infected, or how many folks between ages 15-25 are infected)
- Supports (simulation → data-analytics → simulation) loop
- Interventions and statement assessment questions specified as SQL queries
- New data-centric architecture for interactive epidemic simulation environments
- Decouples data, disease diffusion, intervention and user interaction



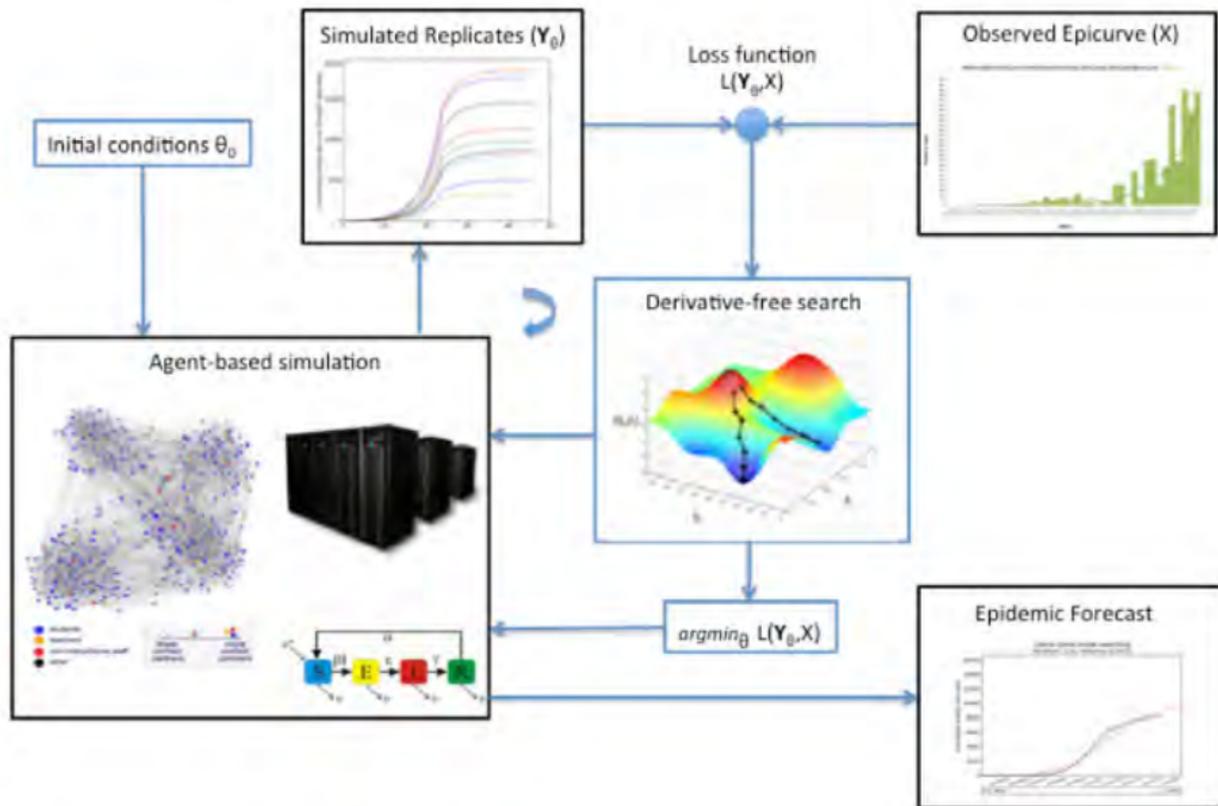
Step 4: Evaluating Policies, Forecasting and Situation Assessment



Calibration and Forecasting

- $\mathcal{X}(1, T) = \langle X(1), \dots, X(T) \rangle$ denote observations till time T . (e.g. incidence rates for the entire population, or attack rates for different regions or subpopulations.)
- *The calibration problem* find a model θ such that the outcomes Y_θ are “close” to \mathcal{X} , using weighted L_1 distance:
$$\min_{\theta} \frac{1}{R} \sum_{r=1}^R \left(\sum_{i=1}^T \alpha^{T-i} |Y_{\theta,r}(i) - X(i)| \right),$$
where $Y_{\theta,r}$ denotes the epicurve for the r th replicate.
- *The forecasting problem*: Given a quantity of interest $Q(\cdot)$ (e.g., number infected), compute the time-series $\mathcal{Q}(1, T+r) = \langle Q(1), \dots, Q(T+r) \rangle$, where $Q(i)$ denotes the value of the quantity at time i and associated confidence probability $p(i)$ for the value to occur.
- *Metrics*: (i) how far ahead in time (r) it projects (ii) how high the confidence ($p(\cdot)$) is (iii) the quantities $Q(\cdot)$ it can project (e.g., peak, time to peak, total infections, etc).

Using derivative free optimization approach



How do network-based causal models helps

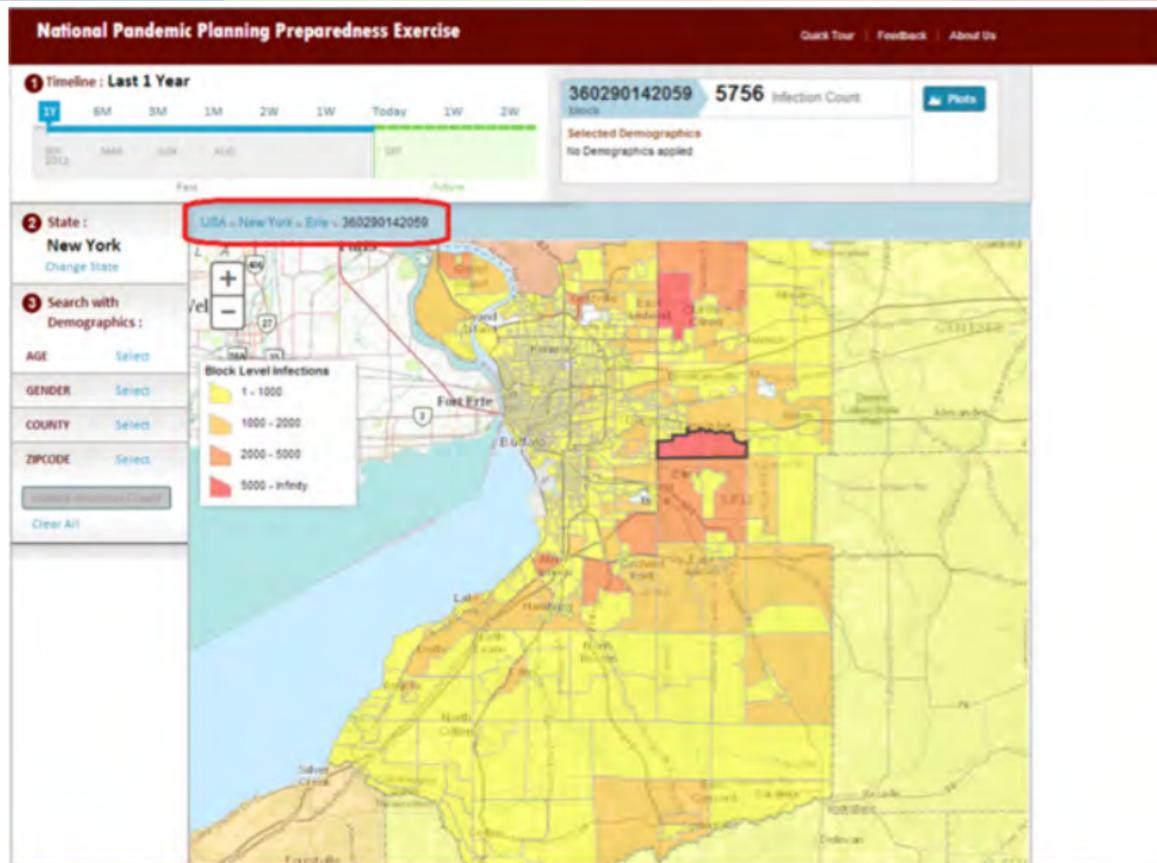
■ Statistical Models

- Specific model/predictor for each data source
- Weights for fusing predictions are learned using cross-validation
- Low computational complexity, produces good short term forecasts.
- Easy to extend when new data sources are found (e.g. weather, flu-near you, Athena)

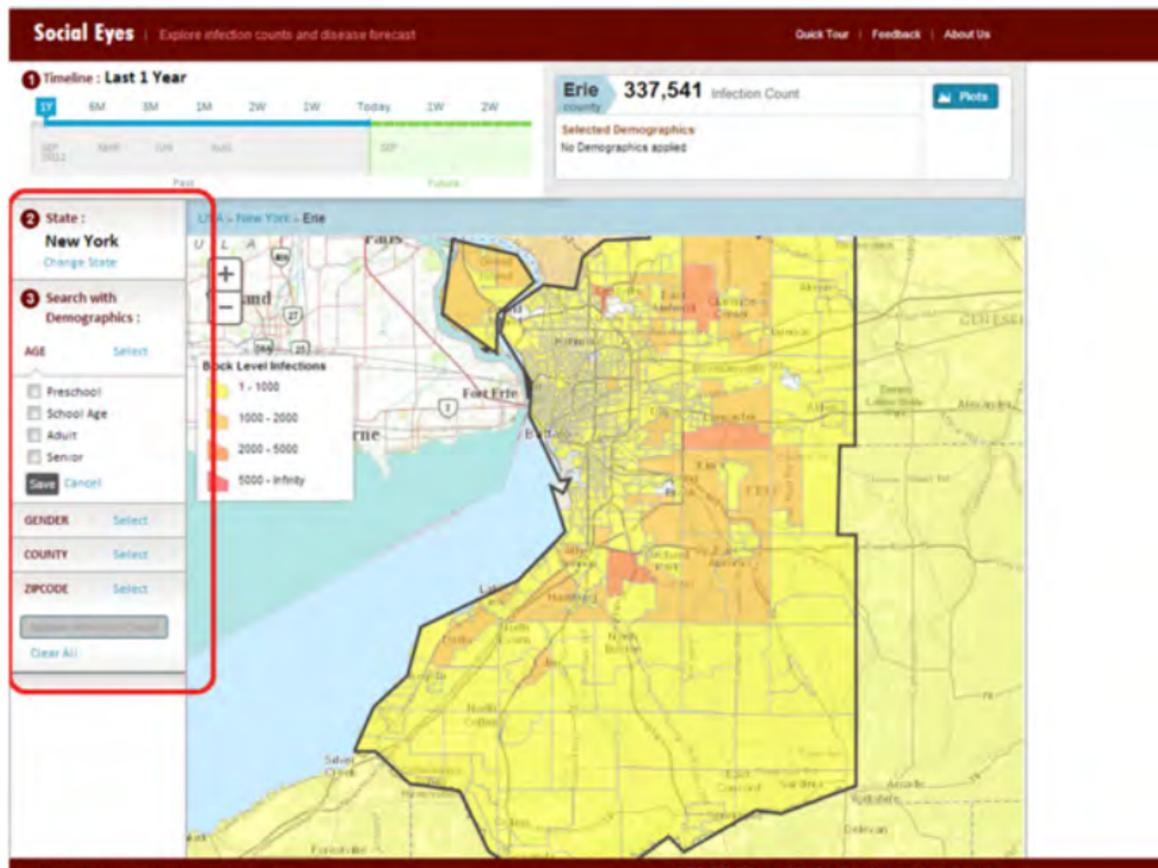
■ Causal Models

- Both ODE (low compute resources) and network-based models (high compute resource) can serve as causal models
- Network models: Simulation + Blackbox optimization+ Machine learning detailed yields *dendograms*
- *Universality*: Dendograms + Spatially explicit social network yields forecast for many reasonable quantities of interest

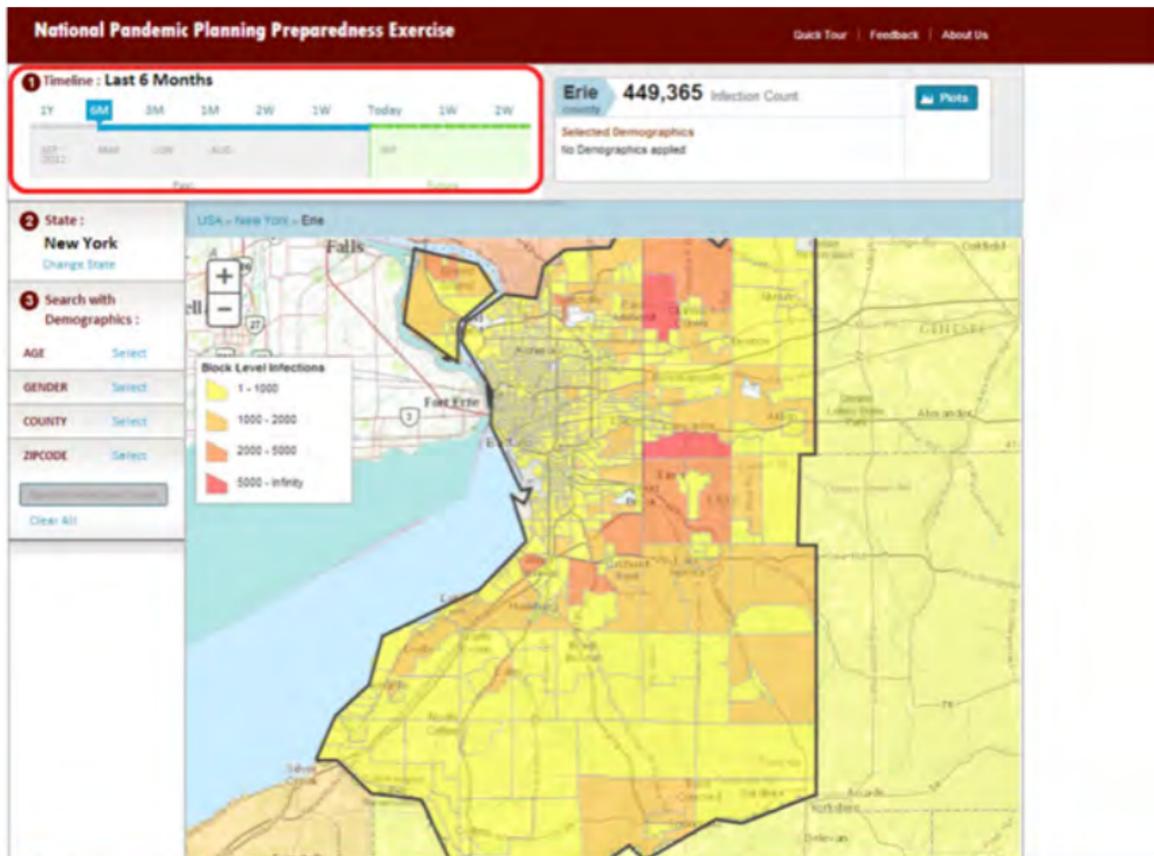
Forecasting using causal models: improved spatial resolution



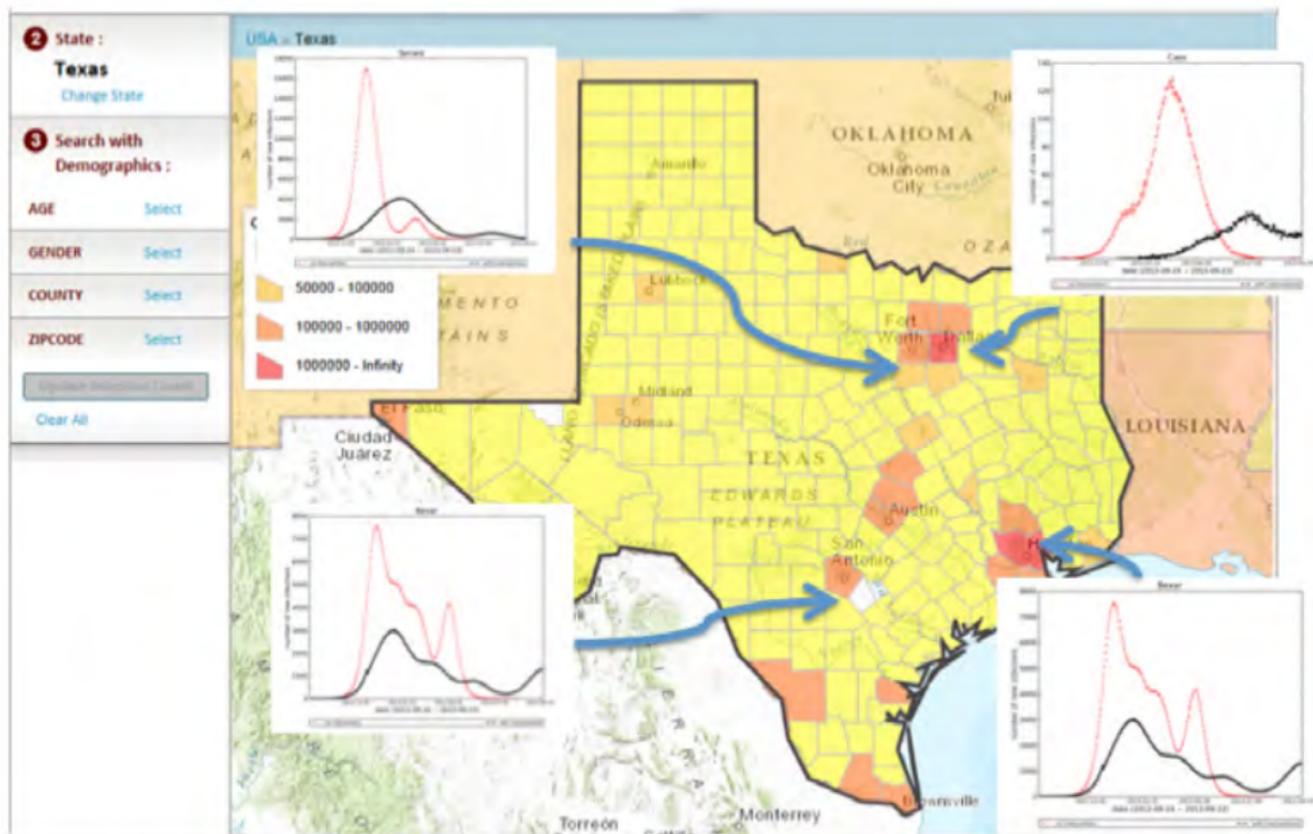
Forecasting using causal models: improved demographic resolution



Forecasting using causal models: improved temporal resolution



Forecasting using causal models: capturing interventions



Outline

- Mathematical models for epidemic spread
- Intervention design as optimization problems
 - Social objective: designing interventions to minimize outbreak (centralized)
 - Social objective with limited compliance: group level interventions (partially centralized)
 - Individual level objective: game-theoretical interventions (decentralized)
 - Combining individual and social objectives: anti-viral distribution problem



Epidemic Analysis problem as a Markov Decision Process

- Computer experiments pertaining to control, resource allocation, planning in epidemiology are best viewed as a Markov decision process (MDP).



Combining social and individual incentives: anti-viral distribution problem

- Policy Problem: Is there an optimum strategy to partition the scarce AV doses between public stockpile administered through hospitals and private stockpile distributed using a market-mechanism
- Measures of Effectiveness: Number of infected, peak infections, cost of recovery, equitable allocation
- Additional issues: How do disease prevalence, individual behavior, network structure, disease dynamics and AV demand co-evolve?



Models of individual behaviors and adaptation

- Isolation based on Prevalence (fear contagion)
 - Entire household isolated when perceived prevalence $>$ threshold
 - Compliance rate: 40%
- Economic Behavior: Demand elasticity based on Prevalence
 - Household demand: $D_{t,h} = \frac{B_{t,h}}{P_t}(1 - e^{-\beta x_t})$
 - Increases with disease prevalence x_t
 - Increases with household budget $B_{t,h}$, decreases with price P_t , and price is linear in remaining supply
 - β reflects risk aversion or prevalence elastic demand to AV.
- Disease Reporting and treatment
 - Anti-virals are administered to individuals who are symptomatic, report clinic and are correctly diagnosed.

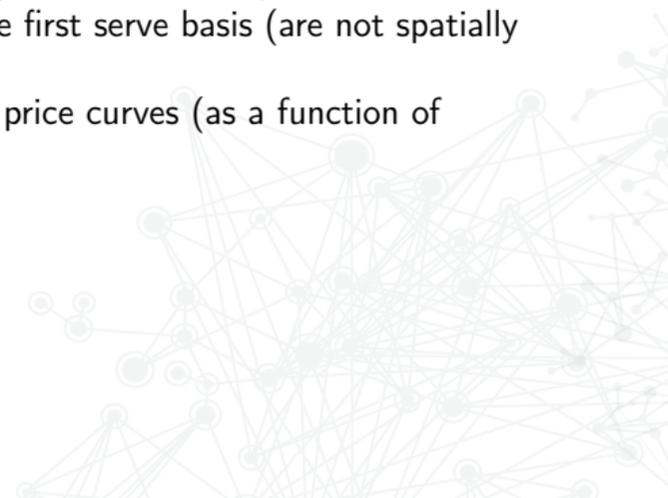
Organizational Behavioral models

- Hospitals

- Total AV supply is 15K: allocated between hospitals and market
- Hospitals: give to diagnosed as infected

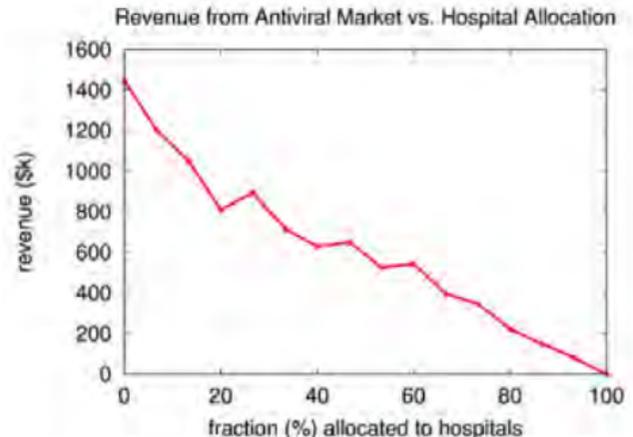
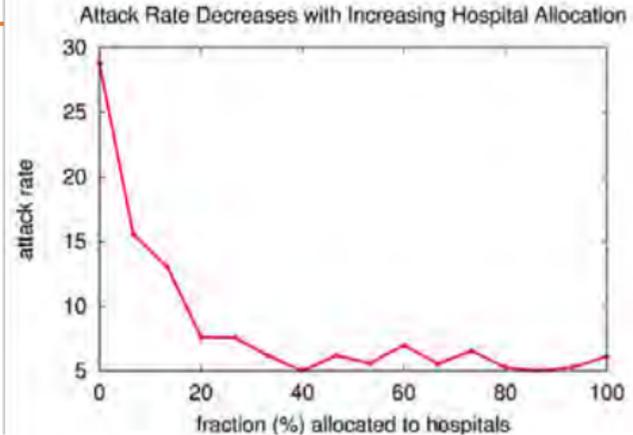
- Markets

- Market: sells to households according to demand and price
- Markets provide A/Vs on a first come first serve basis (are not spatially sensitive in this version)
- Assume a centralized market. Linear price curves (as a function of remaining A/V stock)



Results (I): both Private and Public Distribution are important

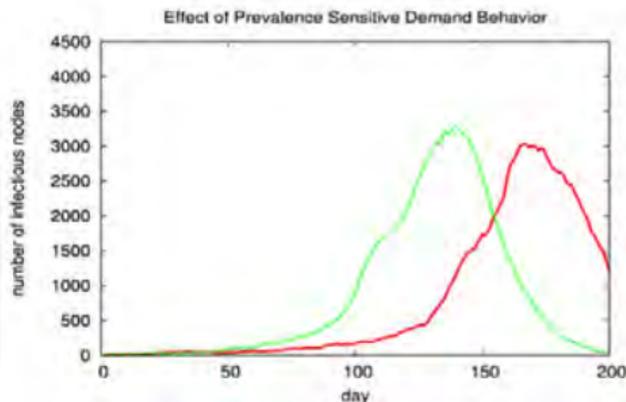
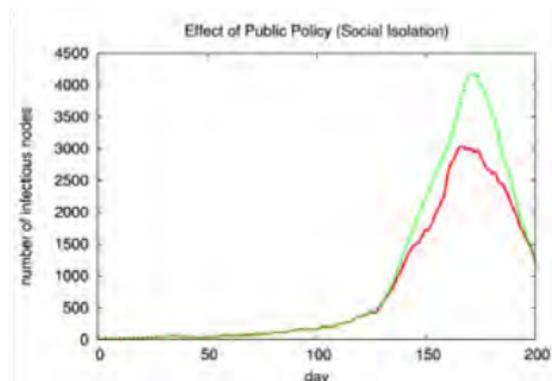
- Suggests optimal allocation strategy of AVs between public and private stockpile
 - Hospitals (public sector) should be given priority
 - If $>$ threshold, the remaining stockpile be distributed via market.
 - Private stockpile useful for individuals who are infectious but not symptomatic
- Optimal split (40% to hospitals, 60% to the market) recovers the cost of antiviral manufacturing if the unit cost is below a bound.



Results (II): Role of Behavioral Adaptations

- Both behavioral adaptations were critical in controlling the epidemic
 - Household isolation reduces the peak infection rate by 30%.
 - Prevalence based demand delays the peak infection rate by 30 days.

Natural behavior adaptation to an epidemic in conjunction with well established logistics (markets + public distribution) reduce and delay the peak infection rate



Step 5: Developing Cyber-ecosystems to support decision making



Cyber-ecosystems: Examples

BSVE by DTRA CB



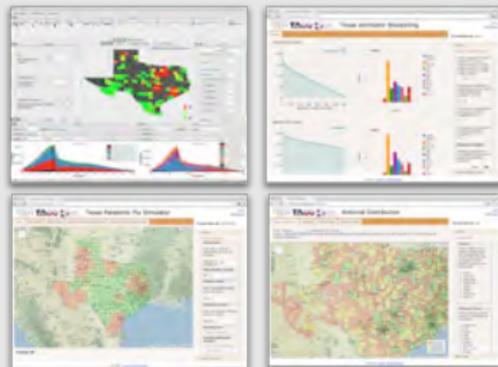
The Biosurveillance Ecosystem (BSVE) at DTRA: a cloud-based, social, self-sustaining web environment to enable real-time biosurveillance

BARD by LANL



Tools to (i) validate/confirm disease surveillance information (ii) rapidly select appropriate epidemiological models for infectious disease prediction, forecasting and monitoring; (iii) provide context and a frame of reference for disease surveillance information

Texas Pandemic tool kit

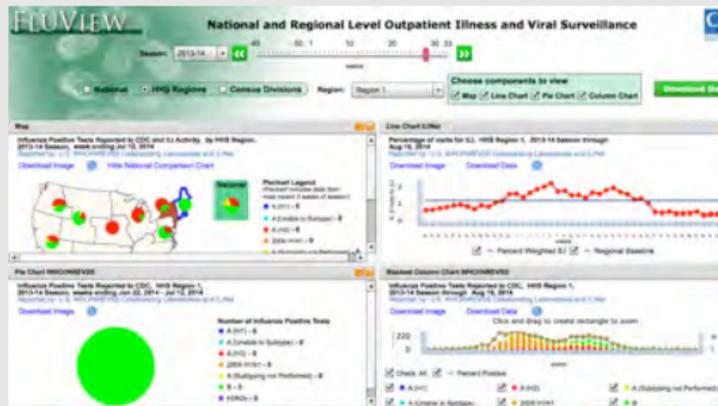


Tools for (i) anti-viral scheduling & distribution; (ii) ventilator stockpiling; (iii) vaccine allocation; (iv) pandemic exercise tool; (v) flu simulator; (vi) sample size calculators for public health labs.

<http://flu.tacc.utexas.edu/>

Cyber-ecosystems: Examples

CDC FluView



<http://www.cdc.gov/flu/weekly/>

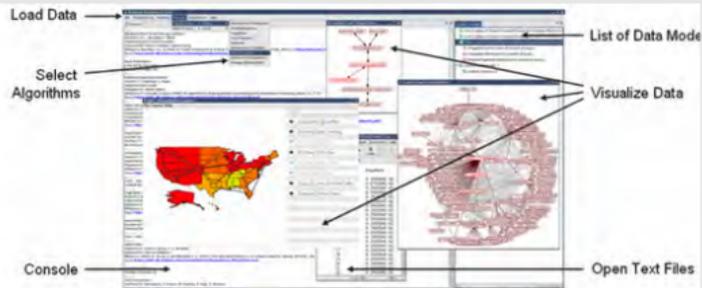
HealthMap



<http://healthmap.org/en/>

EpiC: A Computational Infrastructure for Epidemics (MOBS Lab, Northeastern U.)

EpiC



<http://www.mobs-lab.org/-epic-a-computational-infrastructure.html>

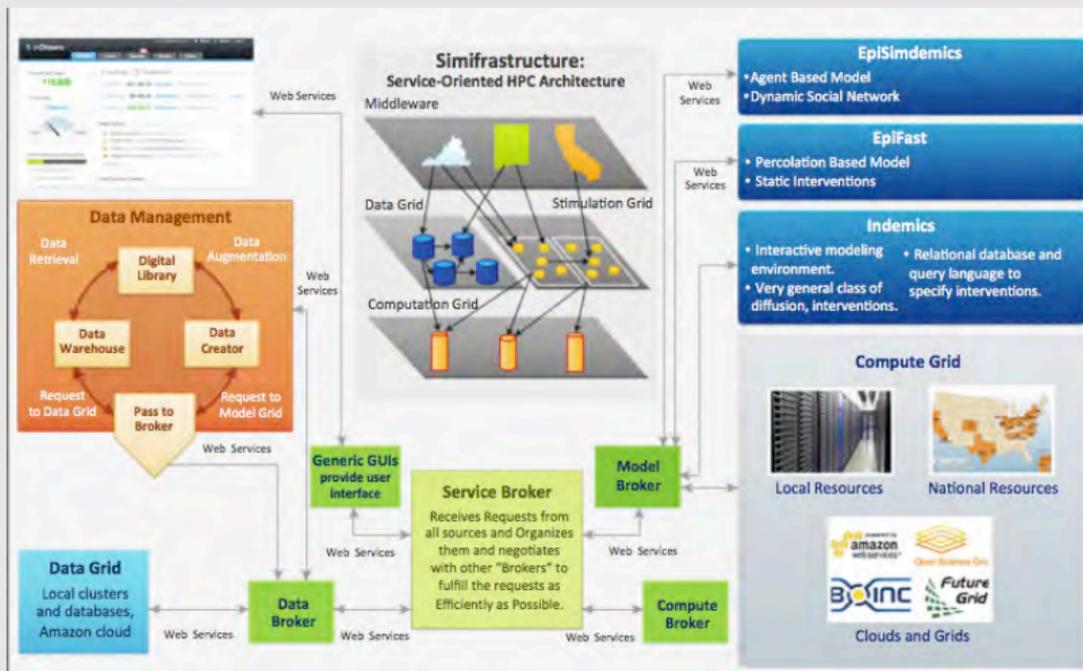
Gleam



www.gleamviz.org

CIEPI: Cyber-infrastructure for computational epidemiology, NDSSL, BI, Virginia Tech

CIEPI Cyber-infrastructure for computational epidemiology by NDSSL



Provides seamless access to high performance computing models, libraries and data

CINET: A cyberinfrastructure for Network Science

- An open access cyberinfrastructure.
 - A web portal that hides the details of computation and data management, thereby minimizing the learning effort required.
- A flexible framework
 - Allows easy extension by integrating off-the-shelf network analysis suites for analysis and visualization; this means new algorithms can be added easily over time.
- A common repository
 - Managing data, models, and results through a digital library that maintains metadata.
- Fostering research, teaching and collaboration
 - Building a broad user base, from multiple disciplines, including incorporation into courses on network science at many different universities.

CINET components

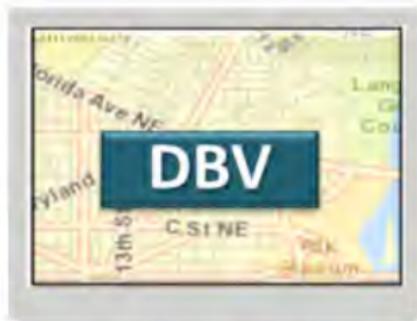
- *Granite*: Structural analysis tool
 - 110+ networks; 18+ network generators.
 - 70+ network algorithms (measures).
 - Adapted from 3 graph libraries: GaLib, SNAP, NetworkX.
 - Visualization of networks (uses Gephi toolkit).
 - Services: Adding new networks, measures
 - *NetScript*: Python-based domain specific language for supporting complex workflows.
- *Edison*: Simulators for broad class of contagion dynamics
 - 20+ networks (graphs).
 - 4 model families.
 - Query system to identify subsets of vertices and edges.
 - Generalized contagion simulator.
- *GDS Calc*: Graph Dynamical System calculator
 - Analyzing the phasic structure of a graph dynamical system (can only deal with smaller networks but complete phase structure).

NDSSL's epidemiological application ecology:<https://www.bi.vt.edu/ndssl/tools>



DSI:DC

DSI:DC is an educational adventure game where players take on the role of a public health agent asked to solve a growing crisis resulting from a disease outbreak. The game focuses on the science and mathematics of infectious disease, the application of computational modeling for decision-making, and the civic and health implications of these actions.



Dynamic Behavior Visualizer

Dynamic Behavior Visualizer (DBV) is an interactive visualization of people, a group of people, or a family used to help understand behaviors and movements over time during a natural or man-made disaster. DBV is used to study the resilience of critical infrastructures such as transportation, communication, and public health.



EDISON

Dynamics on networked populations are useful in understanding social processes on networked populations. Contagion dynamics can take various forms such as epidemics, social protest, smoking and drug use, use of social media, etc. EDISON utilizes big data and data mining to perform social dynamics on networks.

NDSSL's epidemiological application

ecology:<https://www.bi.vt.edu/ndssl/tools>



EpiCaster

Users can view Ebola (or Flu) activity for the past four weeks and view forecast predictions for the next two weeks. They can also view forecast trends and compare them to surveillance data. EpiCaster allows users to see what impact various strategies, such as vaccines and social distancing, have on disease spread.



EpiViewer

EpiViewer is a data repository for epidemiologists. Users can upload and compare Ebola forecasts and surveillance data from a variety of sources and see how forecasts change over time. Users can also load and share their own forecasting predictions.



EpiViz

EpiViz is a highly dynamic system that provides a platform to track and study subjects' decision making and information search strategies, under controlled and repeatable conditions using simulated disease outbreaks. Data visualization supports a multiple views environment and parallel simulation runs.

NDSSL's epidemiological application

ecology:<https://www.bi.vt.edu/ndssl/tools>



Eyes on the Ground

Road conditions can be variable in some of the rural areas in Western Africa. Eyes on the Ground allows people in affected areas to report their road conditions. Other travelers can then view these reports and plan their trips accordingly. This is especially useful when planning the delivery of patients and supplies between cities.



FluCaster

FluCaster is a disease surveillance and situation assessment tool that uses social media crowd sourcing and complex mathematical models to track and predict the spread of communicable diseases. It enables users to see how many people in their area are infected with the flu, displaying area influenza activity similar to a weather forecast.



GDS Calculator

Agent-based simulations are used to understand disease transmission, the spread of social unrest, and the propagation a host of other contagions such as fads, rumors, and influence. Contagions may be spread, for example, by face-to-face interaction and/or electronic means (e.g., social media). Simulation is an effective way to study these dynamics of contagion spread.

NDSSL's epidemiological application

ecology:<https://www.bi.vt.edu/ndssl/tools>



Granite

Networks are an effective abstraction for representing real systems. Consequently, network science is increasingly used in academia and industry to solve problems in many fields. Computations that determine structure properties and dynamical behaviors of networks are useful because they give insights into the characteristics of real systems.



my4Sight

my4Sight uses human computation to enhance disease forecasting. Similar to games like Foldit, this web application allows users to assist computational models by performing tasks that humans are uniquely good at, in this case pattern matching.



PATRIC

PATRIC is the Bacterial Bioinformatics Resource Center, an information system designed to support the biomedical research community's work on bacterial infectious diseases via integration of vital pathogen information with rich data and analysis tools.

NDSSL's epidemiological application

ecology:<https://www.bi.vt.edu/ndssl/tools>



SIBEL

SIBEL allows bioinformatics researchers to design experiments and create analysis for epidemiological disease studies based on realistic social network simulations. It enables improved readiness, planning, and decision making in the domains of public safety and national security by delivering sophisticated modeling and simulation capabilities directly into the hands of the analyst.



SIV

Synthetic Information Viewer (SIV) is a synthetic population visualization tool that allows users to explore demographic information at several levels of resolution - from national to individual. It supports our 2009 version of U.S. data and all international countries NDSSL has constructed, total population of 800+ million.



TranSims

The TRansportation ANalysis SIMulation System is a transportation planning and decision support tool capable of simulating second-by-second movements of every person and every vehicle through the transportation network of a large urban environment. TRANSIMS was the first successful example of high performance computational social sciences and policy informatics.

Three Extensions



Generalized contagions as models of influence and (mis)information



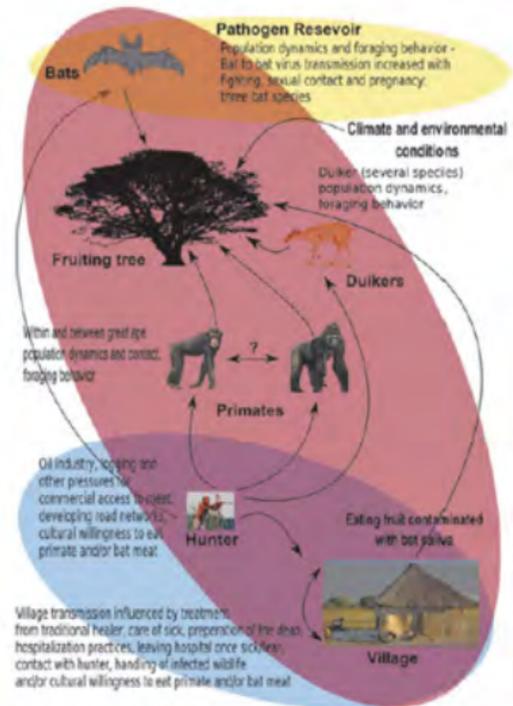
Model	Description	Example Applications
Percolation & extensions: SI/SIS/SIR/Independent cascades	Each red node infects each neighbor independently with some probability	Malware, failures, infections
Complex contagion: threshold and variants	Each node switches to red if at least k neighbors are red	Spread of innovations, peer pressure
Non-monotone multi-threshold models	Thresholds for switching to red and from red to uncolored	More complex social behavior
Voter models	Each node picks the state of a random neighbor	Spread of ideologies

Generalized contagions

- GDS and its generalizations are well suited to capture generalized contagion processes.
- *Example: Social Contagions*
 - *Local Mechanism:* Thresholds, Voter, Linear threshold, Independent cascade, Purely stochastic, Generalized contagion, Cooperative action, Learning, Multi-contagion
 - *Mechanism for social interaction:* Individual (local) interactions (e.g., face-to-face, phone, skype), Joint (group) behaviors (e.g., cadre, team, school, club), Global interactions (e.g., use of social media), & Regional interactions (e.g., TV, news, newspapers, crowds)

Extension 1: Zoonoses and emerging diseases⁶⁹

- **Zoonosis:** Disease that is naturally transmissible from vertebrate animals to humans and vice-versa. Includes all types of pathogenic agents, including bacteria, parasites, fungi, and viruses as causative agents (e.g., Ebola)
- **Spillover:** Process by which a zoonotic pathogen moves from an animal host to a human host.
- Two different R_0 values: capturing human-human and human-animal transmission. Intervention strategies are quite different in the two cases.
- Pharmaceutical interventions are unavailable.



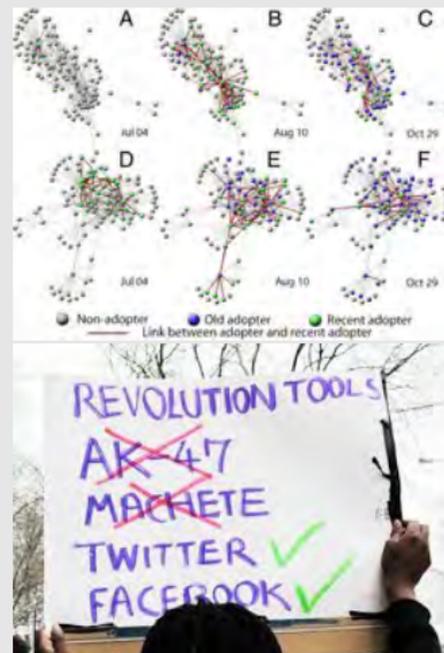
⁶⁹Alexander et al., *Vectore Borne & zoonotic diseases*, 2012

Extension 2: Non-communicable Diseases and social contagions⁷⁰

Obesity is a growing epidemic

- Obesity, Smoking, Memes, product adoption, social unrest: e.g. of epidemic “like” processes.
- Social media important in the recent uprisings, e.g., Arab Spring, Occupy Wall Street. One Egyptian said, “facebook used to set the date, twitter used to share logistics, youtube to show the world, all to connect people.” (Gonzalez-Bailon et al. 2011)
- **Intersim**: High performance computing modeling environment to simulate general contagion processes.

Social contagions



⁷⁰Kuhlman et al. WSC 2012, AAMAS 2014

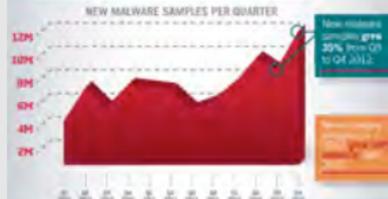
Extension 3: Malware propagation and Internet epidemiology

Malware as generalized contagion

- Amplified as Internet of Things takes hold; the malware ecosystem is becoming rich and diverse.
- **EpiCure**: High performance scalable and expressive modeling environment to study mobile malware in large dynamic networks (Channakesava, et al. IPDPS, 2012)
 - 3.5 million mobile devices in a city as large as Miami can be simulated in 1.5 hours.
 - Model approximations used for bluetooth protocol

Growth of Malware

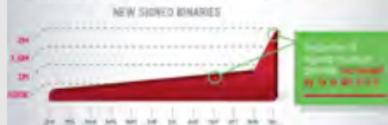
Malware is growing unabated, with no sign of slowing down.



McAfee catalogs over 100,000 new malware samples every day. That's 69 new threats every minute, or about one new threat every second.

Malware is getting more sophisticated.

In addition to the increased volume of threats, the nature of the threats continues to become more dangerous. One of the best ways to circumvent standard system security is to electronically "sign" malware using a stolen or fabricated certificate.



ADVANCED PERSISTENT THREATS

In Q4, a new APT called Project Blotting appeared that attacks consumers and banking institutions. It reportedly stole credit card numbers.

TROJANS

New trojan password-stealing trojans grew 72% in Q4 2012.

<http://www.mcafee.com/us/resources/misc/>

infographic-state-of-malware.pdf

Select region

Back vaccination study **Next**

Details

Replicates 25	Simulated Days 200
Total Cells 1	Model EpiFast

Region

+ Select region

Disease Models

+ Select disease model

Show Cells

A blue arrow button is located to the right of the 'Region' and 'Disease Models' sections.

Back vaccination study **Next**

Region: No Region Attached

Search region

Montgomery County VA

Map showing locations: Parkdale, Blacksburg, Christiansburg, Fosters, Trouton, Shenandoah, and Shenandoah National Park. A red pin is placed on the Blacksburg location.

Cancel **Done**

Select disease model

Back vaccination study Full Access

Details

Realizations	25	Simulated Days	200
Total Cells	1	Model	EpiFast

Region



Disease Models

+ Select disease model

Show Calls

Back vaccination study Full Access

Me All Archived **DiseaseModel: No disease model** + New Disease Model

Details Incubation period Infectious period Symptomatic Proportion

AL_25 Catastrophic flu

AL_25 Mild flu

AL_25 Moderate flu

AL_25 Strong flu

Name AL_25 Catastrophic flu

Modified On Feb 11 2016, 10:52

Owner sample

Transmissibility

Description flu that should infect more than 50% of population (No other flu)

Cancel Save

Specify initial conditions and interventions

Back vaccination study

Details

Replicates: 25
Simulated Days: 200
Total Cells: 1
Model: EpiFast

Region



Disease Models

AL_25 Catastrophic flu

Transmissibility: 0.00006 Symptomatic Proportion: 0.5

Incubation Period



Day	Probability
0	0
1	0.1
2	0.2
3	0.1

Infectious Period



Day	Probability
0	0
1	0
2	0.1
3	0.2
4	0.15
5	0.1
6	0.05

Show Cells

Back vaccination study

Initial Conditions

+ Select initial condition

Enabled Interventions

+ Define interventions

Show Cells

Specify intervention

Back vaccination study

My All Archived Initial Condition (Seday) + New Initial Condition

Seday

Details Condition

Name (1)
Seday

Modified On (1) Feb 11 2016, 10:52

Owner (1) sample

Description (1)
5 vaccinations every day

14 C 1 3 21

Duplicate Cancel Save

Back vaccination study Total Cells 1 View Cells

Enabled Interventions

Summary General Intervention Vaccinate Social Distancing Close Work Close School Pharmaceutical Treatment Pharmaceutical Prophylaxis Dynamic Segmentation

No enabled Interventions

Specify intervention

Intervention Name : senior2060

Subpopulation (i)

Selection: Seniors

Type: Age

Category	Total	Change Percentage
----------	-------	-------------------

Preschool	6.05% (4507)	100% (4507)
-----------	--------------	-------------

School-age	14.9% (11097)	100% (11097)
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Adults	69.9% (52047)	100% (52047)
--------	---------------	--------------

Seniors	9.04% (6725)	100% (6725)
---------	--------------	-------------

Trigger (i)

New

On Day % Infectious Every Day

day15

Name: day15

Value: 15

Duration (i)

Default Exp Simulation Days

Compliance (i)

% Value Sweep (i)

Linear Customized

Initial Value Final Value Increment Value

20

60

10

Go

Efficacy (i)

% Value Sweep (i)

46%

Rate Of Administration (i)

Rate Per Day Unlimited

Summary and concluding remarks



Summary and conclusions

- *Controlling and responding to future pandemics is a hard problem; emerging global trends make it challenging*
 - (i) increased and denser urbanization, (ii) increased local & global travel, (iii) older and immuno-compromised population.
- *Public health epidemiology is a complex system problem.* Epidemics, social-contact networks, individual and collective behavior, and public policies **coevolve** during a pandemic — a system-level understanding must represent these components and their coevolution.
- **Computational Epidemiology:** fascinating field at the intersection of many disciplines. Excellent example of computing for social good.
 - GDS as a unifying framework
 - *Mathematical and computational models and methods are critical in public health epidemiology.*
 - *Advances in computing, big data, and computational thinking have created entirely new opportunities to support real-time epidemiology – a move towards **pervasive computational epidemiology***

Important topics not covered in the tutorial

- Important topics we did not cover
 - Game theory, economics of pandemics, behavioral modeling
 - Uncertainty quantification, Validation and Verification
 - Prediction Markets
- Directions for future research
 - *Ecological Epidemiology*: One-health: understanding epidemiology in a broader context of health and well being across human, animals and plant species: combining ecology and epidemiology
 - *Immunology+Epidemiology*: Current models of disease manifestation are statistical in nature. Use immunological modeling to understand disease progression. Will help understand the role of therapeutics and novel interventions
 - *Phylogeography*: Combining phylogenetics and epidemiology to understand the drift and shift of viruses and their relationship to geography (e.g. Flu, HIV).

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Course notes, data and some of the tools are available on the web:
ndssl.vbi.vt.edu/apps, <http://ndssl.vbi.vt.edu/synthetic-data/>

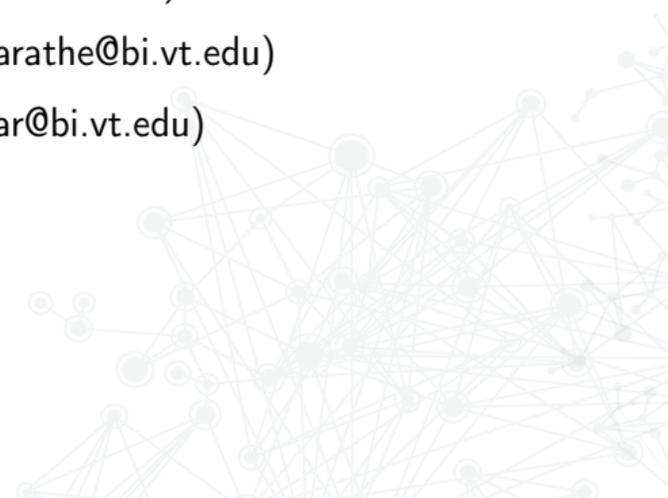
Comments and questions are welcome

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